

Antisense RNAs and DNAs can be used as therapeutic agents for blocking the expression of certain genes *in vivo*. It has already been shown that short antisense oligonucleotides can be imported into cells where they act as inhibitors, despite their low intracellular concentrations caused by their restricted uptake by the cell membrane. (Zamecnik *et al.*, Proc. Natl. Acad. Sci. USA 83:4143-4146 [1986]). The oligonucleotides can be modified to enhance their uptake, e.g. by substituting their negatively charged phosphodiester groups by uncharged groups.

There are a variety of techniques available for introducing nucleic acids into viable cells. The techniques vary depending upon whether the nucleic acid is transferred into cultured cells *in vitro*, or *in vivo* in the cells of the intended host. Techniques suitable for the transfer of nucleic acid into mammalian cells *in vitro* include the use of liposomes, electroporation, microinjection, cell fusion, DEAE-dextran, the calcium phosphate precipitation method, etc. The currently preferred *in vivo* gene transfer techniques include transfection with viral (typically retroviral) vectors and viral coat protein-liposome mediated transfection (Dzau *et al.*, Trends in Biotechnology 11, 205-210 [1993]). In some situations it is desirable to provide the nucleic acid source with an agent that targets the target cells, such as an antibody specific for a cell surface membrane protein or the target cell, a ligand for a receptor on the target cell, etc. Where liposomes are employed, proteins which bind to a cell surface membrane protein associated with endocytosis may be used for targeting and/or to facilitate uptake, e.g. capsid proteins or fragments thereof tropic for a particular cell type, antibodies for proteins which undergo internalization in cycling, proteins that target intracellular localization and enhance intracellular half-life. The technique of receptor-mediated endocytosis is described, for example, by Wu *et al.*, J. Biol. Chem. 262, 4429-4432 (1987); and Wagner *et al.*, Proc. Natl. Acad. Sci. USA 87, 3410-3414 (1990). For review of gene marking and gene therapy protocols see Anderson *et al.*, Science 256, 808-813 (1992).

The PRO polypeptides described herein may also be employed as molecular weight markers for protein electrophoresis purposes.

The nucleic acid molecules encoding the PRO polypeptides or fragments thereof described herein are useful for chromosome identification. In this regard, there exists an ongoing need to identify new chromosome markers, since relatively few chromosome marking reagents, based upon actual sequence data are presently available. Each PRO nucleic acid molecule of the present invention can be used as a chromosome marker.

The PRO polypeptides and nucleic acid molecules of the present invention may also be used for tissue typing, wherein the PRO polypeptides of the present invention may be differentially expressed in one tissue as compared to another. PRO nucleic acid molecules will find use for generating probes for PCR, Northern analysis, Southern analysis and Western analysis.

The PRO polypeptides described herein may also be employed as therapeutic agents. The PRO polypeptides of the present invention can be formulated according to known methods to prepare pharmaceutically useful compositions, whereby the PRO product hereof is combined in admixture with a pharmaceutically acceptable carrier vehicle. Therapeutic formulations are prepared for storage by mixing the active ingredient having the desired degree of purity with optional physiologically acceptable carriers, excipients or stabilizers (Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. (1980)), in the form of lyophilized formulations or aqueous solutions. Acceptable carriers, excipients or stabilizers are nontoxic to recipients at the

dosages and concentrations employed, and include buffers such as phosphate, citrate and other organic acids; antioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone, amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions such as sodium; and/or nonionic surfactants such as TWEENTM, PLURONICSTM or PEG.

The formulations to be used for *in vivo* administration must be sterile. This is readily accomplished by filtration through sterile filtration membranes, prior to or following lyophilization and reconstitution.

Therapeutic compositions herein generally are placed into a container having a sterile access port, for example, an intravenous solution bag or vial having a stopper pierceable by a hypodermic injection needle.

The route of administration is in accord with known methods, e.g. injection or infusion by intravenous, intraperitoneal, intracerebral, intramuscular, intraocular, intraarterial or intralesional routes, topical administration, or by sustained release systems.

Dosages and desired drug concentrations of pharmaceutical compositions of the present invention may vary depending on the particular use envisioned. The determination of the appropriate dosage or route of administration is well within the skill of an ordinary physician. Animal experiments provide reliable guidance for the determination of effective doses for human therapy. Interspecies scaling of effective doses can be performed following the principles laid down by Mordenti, J. and Chappell, W. "The use of interspecies scaling in toxicokinetics" In *Toxicokinetics and New Drug Development*, Yacobi et al., Eds., Pergamon Press, New York 1989, pp. 42-96.

When *in vivo* administration of a PRO polypeptide or agonist or antagonist thereof is employed, normal dosage amounts may vary from about 10 ng/kg to up to 100 mg/kg of mammal body weight or more per day, preferably about 1 µg/kg/day to 10 mg/kg/day, depending upon the route of administration. Guidance as to particular dosages and methods of delivery is provided in the literature; see, for example, U.S. Pat. Nos. 4,657,760; 5,206,344; or 5,225,212. It is anticipated that different formulations will be effective for different treatment compounds and different disorders, that administration targeting one organ or tissue, for example, may necessitate delivery in a manner different from that to another organ or tissue.

Where sustained-release administration of a PRO polypeptide is desired in a formulation with release characteristics suitable for the treatment of any disease or disorder requiring administration of the PRO polypeptide, microencapsulation of the PRO polypeptide is contemplated. Microencapsulation of recombinant proteins for sustained release has been successfully performed with human growth hormone (rhGH), interferon- (rhIFN-), interleukin-2, and MN rgp120. Johnson et al., *Nat. Med.*, 2:795-799 (1996); Yasuda, *Biomed. Ther.*, 27:1221-1223 (1993); Hora et al., *Bio/Technology*, 8:755-758 (1990); Cleland, "Design and Production of Single Immunization Vaccines Using Polylactide Polyglycolide Microsphere Systems," in *Vaccine Design: The Subunit and Adjuvant Approach*, Powell and Newman, eds, (Plenum Press: New York, 1995), pp. 439-462; WO 97/03692, WO 96/40072, WO 96/07399; and U.S. Pat. No. 5,654,010.

The sustained-release formulations of these proteins were developed using poly-lactic-co-glycolic acid (PLGA) polymer due to its biocompatibility and wide range of biodegradable properties. The degradation products of PLGA, lactic and glycolic acids, can be cleared quickly within the human body. Moreover, the degradability of this polymer can be adjusted from months to years depending on its molecular weight and composition. Lewis, "Controlled release of bioactive agents from lactide/glycolide polymer," in: M. Chasin and R. Langer (Eds.), Biodegradable Polymers as Drug Delivery Systems (Marcel Dekker: New York, 1990), pp. 1-41.

This invention encompasses methods of screening compounds to identify those that mimic the PRO polypeptide (agonists) or prevent the effect of the PRO polypeptide (antagonists). Screening assays for antagonist drug candidates are designed to identify compounds that bind or complex with the PRO polypeptides encoded by the genes identified herein, or otherwise interfere with the interaction of the encoded polypeptides with other cellular proteins. Such screening assays will include assays amenable to high-throughput screening of chemical libraries, making them particularly suitable for identifying small molecule drug candidates.

The assays can be performed in a variety of formats, including protein-protein binding assays, biochemical screening assays, immunoassays, and cell-based assays, which are well characterized in the art.

All assays for antagonists are common in that they call for contacting the drug candidate with a PRO polypeptide encoded by a nucleic acid identified herein under conditions and for a time sufficient to allow these two components to interact.

In binding assays, the interaction is binding and the complex formed can be isolated or detected in the reaction mixture. In a particular embodiment, the PRO polypeptide encoded by the gene identified herein or the drug candidate is immobilized on a solid phase, e.g., on a microtiter plate, by covalent or non-covalent attachments. Non-covalent attachment generally is accomplished by coating the solid surface with a solution of the PRO polypeptide and drying. Alternatively, an immobilized antibody, e.g., a monoclonal antibody, specific for the PRO polypeptide to be immobilized can be used to anchor it to a solid surface. The assay is performed by adding the non-immobilized component, which may be labeled by a detectable label, to the immobilized component, e.g., the coated surface containing the anchored component. When the reaction is complete, the non-reacted components are removed, e.g., by washing, and complexes anchored on the solid surface are detected. When the originally non-immobilized component carries a detectable label, the detection of label immobilized on the surface indicates that complexing occurred. Where the originally non-immobilized component does not carry a label, complexing can be detected, for example, by using a labeled antibody specifically binding the immobilized complex.

If the candidate compound interacts with but does not bind to a particular PRO polypeptide encoded by a gene identified herein, its interaction with that polypeptide can be assayed by methods well known for detecting protein-protein interactions. Such assays include traditional approaches, such as, e.g., cross-linking, co-immunoprecipitation, and co-purification through gradients or chromatographic columns. In addition, protein-protein interactions can be monitored by using a yeast-based genetic system described by Fields and co-workers (Fields and Song, Nature (London), 340:245-246 (1989); Chien et al., Proc. Natl. Acad. Sci. USA, 88:9578-9582 (1991)) as disclosed by Chevray and Nathans, Proc. Natl. Acad. Sci. USA, 89: 5789-5793 (1991). Many

transcriptional activators, such as yeast GAL4, consist of two physically discrete modular domains, one acting as the DNA-binding domain, the other one functioning as the transcription-activation domain. The yeast expression system described in the foregoing publications (generally referred to as the "two-hybrid system") takes advantage of this property, and employs two hybrid proteins, one in which the target protein is fused to the DNA-binding domain of GAL4, and another, in which candidate activating proteins are fused to the activation domain. The expression of a GAL1-*lacZ* reporter gene under control of a GAL4-activated promoter depends on reconstitution of GAL4 activity via protein-protein interaction. Colonies containing interacting polypeptides are detected with a chromogenic substrate for β -galactosidase. A complete kit (MATCHMAKER™) for identifying protein-protein interactions between two specific proteins using the two-hybrid technique is commercially available from Clontech. This system can also be extended to map protein domains involved in specific protein interactions as well as to pinpoint amino acid residues that are crucial for these interactions.

Compounds that interfere with the interaction of a gene encoding a PRO polypeptide identified herein and other intra- or extracellular components can be tested as follows: usually a reaction mixture is prepared containing the product of the gene and the intra- or extracellular component under conditions and for a time allowing for the interaction and binding of the two products. To test the ability of a candidate compound to inhibit binding, the reaction is run in the absence and in the presence of the test compound. In addition, a placebo may be added to a third reaction mixture, to serve as positive control. The binding (complex formation) between the test compound and the intra- or extracellular component present in the mixture is monitored as described hereinabove. The formation of a complex in the control reaction(s) but not in the reaction mixture containing the test compound indicates that the test compound interferes with the interaction of the test compound and its reaction partner.

To assay for antagonists, the PRO polypeptide may be added to a cell along with the compound to be screened for a particular activity and the ability of the compound to inhibit the activity of interest in the presence of the PRO polypeptide indicates that the compound is an antagonist to the PRO polypeptide. Alternatively, antagonists may be detected by combining the PRO polypeptide and a potential antagonist with membrane-bound PRO polypeptide receptors or recombinant receptors under appropriate conditions for a competitive inhibition assay. The PRO polypeptide can be labeled, such as by radioactivity, such that the number of PRO polypeptide molecules bound to the receptor can be used to determine the effectiveness of the potential antagonist. The gene encoding the receptor can be identified by numerous methods known to those of skill in the art, for example, ligand panning and FACS sorting. Coligan et al., Current Protocols in Immun., 1(2): Chapter 5 (1991). Preferably, expression cloning is employed wherein polyadenylated RNA is prepared from a cell responsive to the PRO polypeptide and a cDNA library created from this RNA is divided into pools and used to transfect COS cells or other cells that are not responsive to the PRO polypeptide. Transfected cells that are grown on glass slides are exposed to labeled PRO polypeptide. The PRO polypeptide can be labeled by a variety of means including iodination or inclusion of a recognition site for a site-specific protein kinase. Following fixation and incubation, the slides are subjected to autoradiographic analysis. Positive pools are identified and sub-pools are prepared and re-transfected using an interactive sub-pooling and re-screening process, eventually yielding a

single clone that encodes the putative receptor.

As an alternative approach for receptor identification, labeled PRO polypeptide can be photoaffinity-linked with cell membrane or extract preparations that express the receptor molecule. Cross-linked material is resolved by PAGE and exposed to X-ray film. The labeled complex containing the receptor can be excised, resolved into peptide fragments, and subjected to protein micro-sequencing. The amino acid sequence obtained
5 from micro-sequencing would be used to design a set of degenerate oligonucleotide probes to screen a cDNA library to identify the gene encoding the putative receptor.

In another assay for antagonists, mammalian cells or a membrane preparation expressing the receptor would be incubated with labeled PRO polypeptide in the presence of the candidate compound. The ability of the compound to enhance or block this interaction could then be measured.

10 More specific examples of potential antagonists include an oligonucleotide that binds to the fusions of immunoglobulin with PRO polypeptide, and, in particular, antibodies including, without limitation, poly- and monoclonal antibodies and antibody fragments, single-chain antibodies, anti-idiotypic antibodies, and chimeric or humanized versions of such antibodies or fragments, as well as human antibodies and antibody fragments. Alternatively, a potential antagonist may be a closely related protein, for example, a mutated form of the PRO
15 polypeptide that recognizes the receptor but imparts no effect, thereby competitively inhibiting the action of the PRO polypeptide.

Another potential PRO polypeptide antagonist is an antisense RNA or DNA construct prepared using antisense technology, where, e.g., an antisense RNA or DNA molecule acts to block directly the translation of mRNA by hybridizing to targeted mRNA and preventing protein translation. Antisense technology can be used
20 to control gene expression through triple-helix formation or antisense DNA or RNA, both of which methods are based on binding of a polynucleotide to DNA or RNA. For example, the 5' coding portion of the polynucleotide sequence, which encodes the mature PRO polypeptides herein, is used to design an antisense RNA oligonucleotide of from about 10 to 40 base pairs in length. A DNA oligonucleotide is designed to be complementary to a region of the gene involved in transcription (triple helix - see Lee et al., Nucl. Acids Res.,
25 6:3073 (1979); Cooney et al., Science, 241: 456 (1988); Dervan et al., Science, 251:1360 (1991)), thereby preventing transcription and the production of the PRO polypeptide. The antisense RNA oligonucleotide hybridizes to the mRNA *in vivo* and blocks translation of the mRNA molecule into the PRO polypeptide (antisense - Okano, Neurochem., 56:560 (1991); Oligodeoxynucleotides as Antisense Inhibitors of Gene Expression (CRC Press: Boca Raton, FL, 1988). The oligonucleotides described above can also be delivered
30 to cells such that the antisense RNA or DNA may be expressed *in vivo* to inhibit production of the PRO polypeptide. When antisense DNA is used, oligodeoxyribonucleotides derived from the translation-initiationsite, e.g., between about -10 and +10 positions of the target gene nucleotide sequence, are preferred.

Potential antagonists include small molecules that bind to the active site, the receptor binding site, or growth factor or other relevant binding site of the PRO polypeptide, thereby blocking the normal biological
35 activity of the PRO polypeptide. Examples of small molecules include, but are not limited to, small peptides or peptide-like molecules, preferably soluble peptides, and synthetic non-peptidyl organic or inorganic compounds.

Ribozymes are enzymatic RNA molecules capable of catalyzing the specific cleavage of RNA. Ribozymes act by sequence-specific hybridization to the complementary target RNA, followed by endonucleolytic cleavage. Specific ribozyme cleavage sites within a potential RNA target can be identified by known techniques. For further details see, e.g., Rossi, Current Biology, 4:469-471 (1994), and PCT publication No. WO 97/33551 (published September 18, 1997).

5 Nucleic acid molecules in triple-helix formation used to inhibit transcription should be single-stranded and composed of deoxynucleotides. The base composition of these oligonucleotides is designed such that it promotes triple-helix formation via Hoogsteen base-pairing rules, which generally require sizeable stretches of purines or pyrimidines on one strand of a duplex. For further details see, e.g., PCT publication No. WO 97/33551, *supra*.

10 These small molecules can be identified by any one or more of the screening assays discussed hereinabove and/or by any other screening techniques well known for those skilled in the art.

PRO189 can be used in assays with W01A6.1 of *C. Elegans*, phosphodiesterases, transporters and proteins which bind to fatty acids, to determine the relative activities of PRO189 against these proteins. The results can be applied accordingly.

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F. Anti-PRO Antibodies

The present invention further provides anti-PRO antibodies. Exemplary antibodies include polyclonal, monoclonal, humanized, bispecific, and heteroconjugate antibodies.

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1. Polyclonal Antibodies

The anti-PRO antibodies may comprise polyclonal antibodies. Methods of preparing polyclonal antibodies are known to the skilled artisan. Polyclonal antibodies can be raised in a mammal, for example, by one or more injections of an immunizing agent and, if desired, an adjuvant. Typically, the immunizing agent and/or adjuvant will be injected in the mammal by multiple subcutaneous or intraperitoneal injections. The immunizing agent may include the PRO polypeptide or a fusion protein thereof. It may be useful to conjugate the immunizing agent to a protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. Examples of adjuvants which may be employed include Freund's complete adjuvant and MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate).

25 30 The immunization protocol may be selected by one skilled in the art without undue experimentation.

2. Monoclonal Antibodies

The anti-PRO antibodies may, alternatively, be monoclonal antibodies. Monoclonal antibodies may be prepared using hybridoma methods, such as those described by Kohler and Milstein, Nature, 256:495 (1975).

35 In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes may be immunized *in vitro*.

The immunizing agent will typically include the PRO polypeptide or a fusion protein thereof. Generally, either peripheral blood lymphocytes ("PBLs") are used if cells of human origin are desired, or spleen cells or lymph node cells are used if non-human mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell [Goding, Monoclonal Antibodies: Principles and Practice, Academic Press, (1986) pp. 59-103].

- 5 Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells may be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

- Preferred immortalized cell lines are those that fuse efficiently, support stable high level expression of antibody by the selected antibody-producing cells, and are sensitive to a medium such as HAT medium. More preferred immortalized cell lines are murine myeloma lines, which can be obtained, for instance, from the Salk Institute Cell Distribution Center, San Diego, California and the American Type Culture Collection, Manassas, Virginia. Human myeloma and mouse-human heteromyeloma cell lines also have been described for the production of human monoclonal antibodies [Kozbor, J. Immunol., 133:3001 (1984); Brodeur et al., Monoclonal Antibody Production Techniques and Applications, Marcel Dekker, Inc., New York, (1987) pp. 51-63].

- The culture medium in which the hybridoma cells are cultured can then be assayed for the presence of monoclonal antibodies directed against PRO. Preferably, the binding specificity of monoclonal antibodies produced by the hybridoma cells is determined by immunoprecipitation or by an *in vitro* binding assay, such as radioimmunoassay (RIA) or enzyme-linked immunoabsorbent assay (ELISA). Such techniques and assays are known in the art. The binding affinity of the monoclonal antibody can, for example, be determined by the Scatchard analysis of Munson and Pollard, Anal. Biochem., 107:220 (1980).

- 25 After the desired hybridoma cells are identified, the clones may be subcloned by limiting dilution procedures and grown by standard methods [Goding, supra]. Suitable culture media for this purpose include, for example, Dulbecco's Modified Eagle's Medium and RPMI-1640 medium. Alternatively, the hybridoma cells may be grown *in vivo* as ascites in a mammal.

- The monoclonal antibodies secreted by the subclones may be isolated or purified from the culture medium or ascites fluid by conventional immunoglobulin purification procedures such as, for example, protein A-Sepharose, hydroxylapatite chromatography, gel electrophoresis, dialysis, or affinity chromatography.

- The monoclonal antibodies may also be made by recombinant DNA methods, such as those described in U.S. Patent No. 4,816,567. DNA encoding the monoclonal antibodies of the invention can be readily isolated and sequenced using conventional procedures (e.g., by using oligonucleotide probes that are capable of binding specifically to genes encoding the heavy and light chains of murine antibodies). The hybridoma cells of the invention serve as a preferred source of such DNA. Once isolated, the DNA may be placed into expression vectors, which are then transfected into host cells such as simian COS cells, Chinese hamster ovary (CHO) cells,

or myeloma cells that do not otherwise produce immunoglobulin protein, to obtain the synthesis of monoclonal antibodies in the recombinant host cells. The DNA also may be modified, for example, by substituting the coding sequence for human heavy and light chain constant domains in place of the homologous murine sequences [U.S. Patent No. 4,816,567; Morrison et al., *supra*] or by covalently joining to the immunoglobulin coding sequence all or part of the coding sequence for a non-immunoglobulin polypeptide. Such a non-immunoglobulin polypeptide can be substituted for the constant domains of an antibody of the invention, or can be substituted for the variable domains of one antigen-combining site of an antibody of the invention to create a chimeric bivalent antibody.

The antibodies may be monovalent antibodies. Methods for preparing monovalent antibodies are well known in the art. For example, one method involves recombinant expression of immunoglobulin light chain and modified heavy chain. The heavy chain is truncated generally at any point in the Fc region so as to prevent heavy chain crosslinking. Alternatively, the relevant cysteine residues are substituted with another amino acid residue or are deleted so as to prevent crosslinking.

In vitro methods are also suitable for preparing monovalent antibodies. Digestion of antibodies to produce fragments thereof, particularly, Fab fragments, can be accomplished using routine techniques known in the art.

3. Human and Humanized Antibodies

The anti-PRO antibodies of the invention may further comprise humanized antibodies or human antibodies. Humanized forms of non-human (e.g., murine) antibodies are chimeric immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv, Fab, Fab', F(ab')₂ or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. Humanized antibodies include human immunoglobulins (recipient antibody) in which residues from a complementary determining region (CDR) of the recipient are replaced by residues from a CDR of a non-human species (donor antibody) such as mouse, rat or rabbit having the desired specificity, affinity and capacity. In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies may also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, the humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the FR regions are those of a human immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin [Jones et al., *Nature*, 321:522-525 (1986); Riechmann et al., *Nature*, 332:323-329 (1988); and Presta, *Curr. Op. Struct. Biol.*, 2:593-596 (1992)].

Methods for humanizing non-human antibodies are well known in the art. Generally, a humanized antibody has one or more amino acid residues introduced into it from a source which is non-human. These non-human amino acid residues are often referred to as "import" residues, which are typically taken from an "import" variable domain. Humanization can be essentially performed following the method of Winter and co-workers

[Jones et al., Nature, 321:522-525 (1986); Riechmann et al., Nature, 332:323-327 (1988); Verhoeyen et al., Science, 239:1534-1536 (1988)], by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. Accordingly, such "humanized" antibodies are chimeric antibodies (U.S. Patent No. 4,816,567), wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species. In practice, humanized antibodies are typically human antibodies in which some CDR residues and possibly some FR residues are substituted by residues from analogous sites in rodent antibodies.

Human antibodies can also be produced using various techniques known in the art, including phage display libraries [Hoogenboom and Winter, J. Mol. Biol., 227:381 (1991); Marks et al., J. Mol. Biol., 222:581 (1991)]. The techniques of Cole et al. and Boerner et al. are also available for the preparation of human monoclonal antibodies (Cole et al., Monoclonal Antibodies and Cancer Therapy, Alan R. Liss, p. 77 (1985) and Boerner et al., J. Immunol., 147(1):86-95 (1991)]. Similarly, human antibodies can be made by introducing of human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in all respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, for example, in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in the following scientific publications: Marks et al., Bio/Technology 10, 779-783 (1992); Lonberg et al., Nature 368 856-859 (1994); Morrison, Nature 368, 812-13 (1994); Fishwild et al., Nature Biotechnology 14, 845-51 (1996); Neuberger, Nature Biotechnology 14, 826 (1996); Lonberg and Huszar, Intern. Rev. Immunol. 13 65-93 (1995).

4. Bispecific Antibodies

Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens. In the present case, one of the binding specificities is for the PRO, the other one is for any other antigen, and preferably for a cell-surface protein or receptor or receptor subunit.

Methods for making bispecific antibodies are known in the art. Traditionally, the recombinant production of bispecific antibodies is based on the co-expression of two immunoglobulin heavy-chain/light-chain pairs, where the two heavy chains have different specificities [Milstein and Cuello, Nature, 305:537-539 (1983)]. Because of the random assortment of immunoglobulin heavy and light chains, these hybridomas (quadromas) produce a potential mixture of ten different antibody molecules, of which only one has the correct bispecific structure. The purification of the correct molecule is usually accomplished by affinity chromatography steps. Similar procedures are disclosed in WO 93/08829, published 13 May 1993, and in Traunecker et al., EMBO J., 10:3655-3659 (1991).

Antibody variable domains with the desired binding specificities (antibody-antigen combining sites) can be fused to immunoglobulin constant domain sequences. The fusion preferably is with an immunoglobulin heavy-chain constant domain, comprising at least part of the hinge, CH2, and CH3 regions. It is preferred to have the first heavy-chain constant region (CH1) containing the site necessary for light-chain binding present in

at least one of the fusions. DNAs encoding the immunoglobulin heavy-chain fusions and, if desired, the immunoglobulin light chain, are inserted into separate expression vectors, and are co-transfected into a suitable host organism. For further details of generating bispecific antibodies see, for example, Suresh et al., Methods in Enzymology, 121:210 (1986).

According to another approach described in WO 96/27011, the interface between a pair of antibody
5 molecules can be engineered to maximize the percentage of heterodimers which are recovered from recombinant cell culture. The preferred interface comprises at least a part of the CH3 region of an antibody constant domain. In this method, one or more small amino acid side chains from the interface of the first antibody molecule are replaced with larger side chains (e.g. tyrosine or tryptophan). Compensatory "cavities" of identical or similar size to the large side chain(s) are created on the interface of the second antibody molecule by replacing large
10 amino acid side chains with smaller ones (e.g. alanine or threonine). This provides a mechanism for increasing the yield of the heterodimer over other unwanted end-products such as homodimers.

Bispecific antibodies can be prepared as full length antibodies or antibody fragments (e.g. F(ab')₂ bispecific antibodies). Techniques for generating bispecific antibodies from antibody fragments have been described in the literature. For example, bispecific antibodies can be prepared using chemical
15 linkage. Brennan *et al.*, Science 229:81 (1985) describe a procedure wherein intact antibodies are proteolytically cleaved to generate F(ab')₂ fragments. These fragments are reduced in the presence of the dithiol complexing agent sodium arsenite to stabilize vicinal dithiols and prevent intermolecular disulfide formation. The Fab' fragments generated are then converted to thionitrobenzoate (TNB) derivatives. One of the Fab'-TNB derivatives is then reconverted to the Fab'-thiol by reduction with mercaptoethylamine and is mixed with an
20 equimolar amount of the other Fab'-TNB derivative to form the bispecific antibody. The bispecific antibodies produced can be used as agents for the selective immobilization of enzymes.

Fab' fragments may be directly recovered from *E. coli* and chemically coupled to form bispecific antibodies. Shalaby *et al.*, J. Exp. Med. 175:217-225 (1992) describe the production of a fully humanized bispecific antibody F(ab')₂ molecule. Each Fab' fragment was separately secreted from *E. coli* and subjected
25 to directed chemical coupling *in vitro* to form the bispecific antibody. The bispecific antibody thus formed was able to bind to cells overexpressing the ErbB2 receptor and normal human T cells, as well as trigger the lytic activity of human cytotoxic lymphocytes against human breast tumor targets.

Various technique for making and isolating bispecific antibody fragments directly from recombinant cell culture have also been described. For example, bispecific antibodies have been produced using leucine zippers.
30 Kostelny *et al.*, J. Immunol. 148(5):1547-1553 (1992). The leucine zipper peptides from the Fos and Jun proteins were linked to the Fab' portions of two different antibodies by gene fusion. The antibody homodimers were reduced at the hinge region to form monomers and then re-oxidized to form the antibody heterodimers. This method can also be utilized for the production of antibody homodimers. The "diabody" technology described by Hollinger *et al.*, Proc. Natl. Acad. Sci. USA 90:6444-6448 (1993) has provided an alternative
35 mechanism for making bispecific antibody fragments. The fragments comprise a heavy-chain variable domain (V_H) connected to a light-chain variable domain (V_L) by a linker which is too short to allow pairing between the two domains on the same chain. Accordingly, the V_H and V_L domains of one fragment are forced to pair with

the complementary V_L and V_H domains of another fragment, thereby forming two antigen-binding sites. Another strategy for making bispecific antibody fragments by the use of single-chain Fv (sFv) dimers has also been reported. See, Gruber *et al.*, *J. Immunol.* 152:5368 (1994).

Antibodies with more than two valencies are contemplated. For example, trispecific antibodies can be prepared. Tutt *et al.*, *J. Immunol.* 147:60 (1991).

- 5 Exemplary bispecific antibodies may bind to two different epitopes on a given PRO polypeptide herein. Alternatively, an anti-PRO polypeptide arm may be combined with an arm which binds to a triggering molecule on a leukocyte such as a T-cell receptor molecule (e.g. CD2, CD3, CD28, or B7), or Fc receptors for IgG (FcγR), such as FcγRI (CD64), FcγRII (CD32) and FcγRIII (CD16) so as to focus cellular defense mechanisms to the cell expressing the particular PRO polypeptide. Bispecific antibodies may also be used to localize
10 cytotoxic agents to cells which express a particular PRO polypeptide. These antibodies possess a PRO-binding arm and an arm which binds a cytotoxic agent or a radionuclide chelator, such as EOTUBE, DPTA, DOTA, or TETA. Another bispecific antibody of interest binds the PRO polypeptide and further binds tissue factor (TF).

15 5. Heteroconjugate Antibodies

- Heteroconjugate antibodies are also within the scope of the present invention. Heteroconjugate antibodies are composed of two covalently joined antibodies. Such antibodies have, for example, been proposed to target immune system cells to unwanted cells [U.S. Patent No. 4,676,980], and for treatment of HIV infection [WO 91/00360; WO 92/200373; EP 03089]. It is contemplated that the antibodies may be prepared *in vitro*
20 using known methods in synthetic protein chemistry, including those involving crosslinking agents. For example, immunotoxins may be constructed using a disulfide exchange reaction or by forming a thioether bond. Examples of suitable reagents for this purpose include iminothiolate and methyl-4-mercaptobutyrimidate and those disclosed, for example, in U.S. Patent No. 4,676,980.

25 6. Effector Function Engineering

- It may be desirable to modify the antibody of the invention with respect to effector function, so as to enhance, e.g., the effectiveness of the antibody in treating cancer. For example, cysteine residue(s) may be introduced into the Fc region, thereby allowing interchain disulfide bond formation in this region. The homodimeric antibody thus generated may have improved internalization capability and/or increased
30 complement-mediated cell killing and antibody-dependent cellular cytotoxicity (ADCC). See Caron *et al.*, *J. Exp Med.*, 176: 1191-1195 (1992) and Shopes, *J. Immunol.*, 148: 2918-2922 (1992). Homodimeric antibodies with enhanced anti-tumor activity may also be prepared using heterobifunctional cross-linkers as described in Wolff *et al.* *Cancer Research*, 53: 2560-2565 (1993). Alternatively, an antibody can be engineered that has dual Fc regions and may thereby have enhanced complement lysis and ADCC capabilities. See Stevenson *et al.*, *Anti-Cancer Drug Design*, 3: 219-230 (1989).

7. Immunoconjugates

The invention also pertains to immunoconjugates comprising an antibody conjugated to a cytotoxic agent such as a chemotherapeutic agent, toxin (*e.g.*, an enzymatically active toxin of bacterial, fungal, plant, or animal origin, or fragments thereof), or a radioactive isotope (*i.e.*, a radioconjugate).

Chemotherapeutic agents useful in the generation of such immunoconjugates have been described above.

- 5 Enzymatically active toxins and fragments thereof that can be used include diphtheria A chain, nonbinding active fragments of diphtheria toxin, exotoxin A chain (from *Pseudomonas aeruginosa*), ricin A chain, abrin A chain, modeccin A chain, alpha-sarcin, *Aleurites fordii* proteins, dianthin proteins, *Phytolacca americana* proteins (PAPI, PAPII, and PAP-S), momordica charantia inhibitor, curcin, crotin, sapaonaria officinalis inhibitor, gelonin, mitogellin, restrictocin, phenomycin, enomycin, and the tricothecenes. A variety of radionuclides are
10 available for the production of radioconjugated antibodies. Examples include ^{212}Bi , ^{131}I , ^{131}In , ^{90}Y , and ^{186}Re .

- Conjugates of the antibody and cytotoxic agent are made using a variety of bifunctional protein-coupling agents such as N-succinimidyl-3-(2-pyridyldithiol) propionate (SPDP), iminothiolane (IT), bifunctional derivatives of imidoesters (such as dimethyl adipimidate HCL), active esters (such as disuccinimidyl suberate), aldehydes (such as glutaraldehyde), bis-azido compounds (such as bis (p-azidobenzoyl) hexanediamine), bis-
15 diazonium derivatives (such as bis-(p-diazoniumbenzoyl)-ethylenediamine), diisocyanates (such as tolyene 2,6-diisocyanate), and bis-active fluorine compounds (such as 1,5-difluoro-2,4-dinitrobenzene). For example, a ricin immunotoxin can be prepared as described in Vitetta *et al.*, Science, **238**: 1098 (1987). Carbon-14-labeled 1-isothiocyanatobenzyl-3-methyldiethylene triaminepentaacetic acid (MX-DTPA) is an exemplary chelating agent for conjugation of radionucleotide to the antibody. See WO94/11026.

- 20 In another embodiment, the antibody may be conjugated to a "receptor" (such streptavidin) for utilization in tumor pretargeting wherein the antibody-receptor conjugate is administered to the patient, followed by removal of unbound conjugate from the circulation using a clearing agent and then administration of a "ligand" (*e.g.*, avidin) that is conjugated to a cytotoxic agent (*e.g.*, a radionucleotide).

25 8. Immunoliposomes

- The antibodies disclosed herein may also be formulated as immunoliposomes. Liposomes containing the antibody are prepared by methods known in the art, such as described in Epstein *et al.*, Proc. Natl. Acad. Sci. USA, **82**: 3688 (1985); Hwang *et al.*, Proc. Natl. Acad. Sci. USA, **77**: 4030 (1980); and U.S. Pat. Nos. 4,485,045 and 4,544,545. Liposomes with enhanced circulation time are disclosed in U.S. Patent No.
30 5,013,556.

- Particularly useful liposomes can be generated by the reverse-phase evaporation method with a lipid composition comprising phosphatidylcholine, cholesterol, and PEG-derivatized phosphatidylethanolamine (PEG-PE). Liposomes are extruded through filters of defined pore size to yield liposomes with the desired diameter. Fab' fragments of the antibody of the present invention can be conjugated to the liposomes as described in Martin
35 *et al.*, J. Biol. Chem., **257**: 286-288 (1982) via a disulfide-interchange reaction. A chemotherapeutic agent (such as Doxorubicin) is optionally contained within the liposome. See Gabizon *et al.*, J. National Cancer Inst., **81**(19): 1484 (1989).

9. Pharmaceutical Compositions of Antibodies

Antibodies specifically binding a PRO polypeptide identified herein, as well as other molecules identified by the screening assays disclosed hereinbefore, can be administered for the treatment of various disorders in the form of pharmaceutical compositions.

If the PRO polypeptide is intracellular and whole antibodies are used as inhibitors, internalizing antibodies are preferred. However, lipofections or liposomes can also be used to deliver the antibody, or an antibody fragment, into cells. Where antibody fragments are used, the smallest inhibitory fragment that specifically binds to the binding domain of the target protein is preferred. For example, based upon the variable-region sequences of an antibody, peptide molecules can be designed that retain the ability to bind the target protein sequence. Such peptides can be synthesized chemically and/or produced by recombinant DNA technology. See, e.g., Marasco *et al.*, Proc. Natl. Acad. Sci. USA, 90: 7889-7893 (1993). The formulation herein may also contain more than one active compound as necessary for the particular indication being treated, preferably those with complementary activities that do not adversely affect each other. Alternatively, or in addition, the composition may comprise an agent that enhances its function, such as, for example, a cytotoxic agent, cytokine, chemotherapeutic agent, or growth-inhibitory agent. Such molecules are suitably present in combination in amounts that are effective for the purpose intended.

The active ingredients may also be entrapped in microcapsules prepared, for example, by coacervation techniques or by interfacial polymerization, for example, hydroxymethylcellulose or gelatin-microcapsules and poly-(methylmethacrylate) microcapsules, respectively, in colloidal drug delivery systems (for example, liposomes, albumin microspheres, microemulsions, nano-particles, and nanocapsules) or in macroemulsions. Such techniques are disclosed in Remington's Pharmaceutical Sciences, *supra*.

The formulations to be used for *in vivo* administration must be sterile. This is readily accomplished by filtration through sterile filtration membranes.

Sustained-release preparations may be prepared. Suitable examples of sustained-release preparations include semipermeable matrices of solid hydrophobic polymers containing the antibody, which matrices are in the form of shaped articles, e.g., films, or microcapsules. Examples of sustained-release matrices include polyesters, hydrogels (for example, poly(2-hydroxyethyl-methacrylate), or poly(vinylalcohol)), polylactides (U.S. Pat. No. 3,773,919), copolymers of L-glutamic acid and γ ethyl-L-glutamate, non-degradable ethylene-vinyl acetate, degradable lactic acid-glycolic acid copolymers such as the LUPRON DEPOT™ (injectable microspheres composed of lactic acid-glycolic acid copolymer and leuprolide acetate), and poly-D-(-)-3-hydroxybutyric acid. While polymers such as ethylene-vinyl acetate and lactic acid-glycolic acid enable release of molecules for over 100 days, certain hydrogels release proteins for shorter time periods. When encapsulated antibodies remain in the body for a long time, they may denature or aggregate as a result of exposure to moisture at 37°C, resulting in a loss of biological activity and possible changes in immunogenicity. Rational strategies can be devised for stabilization depending on the mechanism involved. For example, if the aggregation mechanism is discovered to be intermolecular S-S bond formation through thio-disulfide interchange, stabilization may be achieved by modifying sulfhydryl residues, lyophilizing from acidic solutions, controlling moisture content, using appropriate additives, and developing specific polymer matrix compositions.

G. Uses for anti-PRO Antibodies

The anti-PRO antibodies of the invention have various utilities. For example, anti-PRO antibodies may be used in diagnostic assays for PRO, *e.g.*, detecting its expression in specific cells, tissues, or serum. Various diagnostic assay techniques known in the art may be used, such as competitive binding assays, direct or indirect sandwich assays and immunoprecipitation assays conducted in either heterogeneous or homogeneous phases [Zola, Monoclonal Antibodies: A Manual of Techniques, CRC Press, Inc. (1987) pp. 147-158]. The antibodies used in the diagnostic assays can be labeled with a detectable moiety. The detectable moiety should be capable of producing, either directly or indirectly, a detectable signal. For example, the detectable moiety may be a radioisotope, such as ^3H , ^{14}C , ^{32}P , ^{35}S , or ^{125}I , a fluorescent or chemiluminescent compound, such as fluorescein isothiocyanate, rhodamine, or luciferin, or an enzyme, such as alkaline phosphatase, beta-galactosidase or horseradish peroxidase. Any method known in the art for conjugating the antibody to the detectable moiety may be employed, including those methods described by Hunter et al., Nature, 144:945 (1962); David et al., Biochemistry, 13:1014 (1974); Pain et al., J. Immunol. Meth., 40:219 (1981); and Nygren, J. Histochem. and Cytochem., 30:407 (1982).

Anti-PRO antibodies also are useful for the affinity purification of PRO from recombinant cell culture or natural sources. In this process, the antibodies against PRO are immobilized on a suitable support, such as Sephadex resin or filter paper, using methods well known in the art. The immobilized antibody then is contacted with a sample containing the PRO to be purified, and thereafter the support is washed with a suitable solvent that will remove substantially all the material in the sample except the PRO, which is bound to the immobilized antibody. Finally, the support is washed with another suitable solvent that will release the PRO from the antibody.

The following examples are offered for illustrative purposes only, and are not intended to limit the scope of the present invention in any way.

All patent and literature references cited in the present specification are hereby incorporated by reference in their entirety.

EXAMPLES

Commercially available reagents referred to in the examples were used according to manufacturer's instructions unless otherwise indicated. The source of those cells identified in the following examples, and throughout the specification, by ATCC accession numbers is the American Type Culture Collection, Manassas, VA.

EXAMPLE 1: Extracellular Domain Homology Screening to Identify Novel Polypeptides and cDNA Encoding Therefor

The extracellular domain (ECD) sequences (including the secretion signal sequence, if any) from about 950 known secreted proteins from the Swiss-Prot public database were used to search EST databases. The EST databases included public databases (*e.g.*, Dayhoff, GenBank), and proprietary databases (*e.g.* LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program WU-BLAST-2

(Altschul et al., Methods in Enzymology 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequences. Those comparisons with a Blast score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, WA).

5 Using this extracellular domain homology screen, consensus DNA sequences were assembled relative to the other identified EST sequences using phrap. In addition, the consensus DNA sequences obtained were often (but not always) extended using repeated cycles of WU-BLAST-2 and phrap to extend the consensus sequence as far as possible using the sources of EST sequences discussed above.

Based upon the consensus sequences obtained as described above, oligonucleotides were then synthesized and used to identify by PCR a cDNA library that contained the sequence of interest and for use as probes to isolate a clone of the full-length coding sequence for a PRO polypeptide. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per
10 Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized
20 appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

EXAMPLE 2: Isolation of cDNA clones by Amylase Screening

25 1. Preparation of oligo dT primed cDNA library

mRNA was isolated from a human tissue of interest using reagents and protocols from Invitrogen, San Diego, CA (Fast Track 2). This RNA was used to generate an oligo dT primed cDNA library in the vector pRK5D using reagents and protocols from Life Technologies, Gaithersburg, MD (Super Script Plasmid System). In this procedure, the double stranded cDNA was sized to greater than 1000 bp and the SalI/NotI linked cDNA
30 was cloned into XhoI/NotI cleaved vector. pRK5D is a cloning vector that has an sp6 transcription initiation site followed by an SfiI restriction enzyme site preceding the XhoI/NotI cDNA cloning sites.

2. Preparation of random primed cDNA library

A secondary cDNA library was generated in order to preferentially represent the 5' ends of the primary
35 cDNA clones. Sp6 RNA was generated from the primary library (described above), and this RNA was used to generate a random primed cDNA library in the vector pSST-AMY.0 using reagents and protocols from Life Technologies (Super Script Plasmid System, referenced above). In this procedure the double stranded cDNA

was sized to 500-1000 bp, linked with blunt to NotI adaptors, cleaved with SfiI, and cloned into SfiI/NotI cleaved vector. pSST-AMY.0 is a cloning vector that has a yeast alcohol dehydrogenase promoter preceding the cDNA cloning sites and the mouse amylase sequence (the mature sequence without the secretion signal) followed by the yeast alcohol dehydrogenase terminator, after the cloning sites. Thus, cDNAs cloned into this vector that are fused in frame with amylase sequence will lead to the secretion of amylase from appropriately transfected yeast colonies.

3. Transformation and Detection

DNA from the library described in paragraph 2 above was chilled on ice to which was added electrocompetent DH10B bacteria (Life Technologies, 20 ml). The bacteria and vector mixture was then electroporated as recommended by the manufacturer. Subsequently, SOC media (Life Technologies, 1 ml) was added and the mixture was incubated at 37°C for 30 minutes. The transformants were then plated onto 20 standard 150 mm LB plates containing ampicillin and incubated for 16 hours (37°C). Positive colonies were scraped off the plates and the DNA was isolated from the bacterial pellet using standard protocols, e.g. CsCl-gradient. The purified DNA was then carried on to the yeast protocols below.

The yeast methods were divided into three categories: (1) Transformation of yeast with the plasmid/cDNA combined vector; (2) Detection and isolation of yeast clones secreting amylase; and (3) PCR amplification of the insert directly from the yeast colony and purification of the DNA for sequencing and further analysis.

The yeast strain used was HD56-5A (ATCC-90785). This strain has the following genotype: MAT alpha, ura3-52, leu2-3, leu2-112, his3-11, his3-15, MAL⁺, SUC⁺, GAL⁺. Preferably, yeast mutants can be employed that have deficient post-translational pathways. Such mutants may have translocation deficient alleles in *sec71*, *sec72*, *sec62*, with truncated *sec71* being most preferred. Alternatively, antagonists (including antisense nucleotides and/or ligands) which interfere with the normal operation of these genes, other proteins implicated in this post translation pathway (e.g., SEC61p, SEC72p, SEC62p, SEC63p, TDJ1p or SSA1p-4p) or the complex formation of these proteins may also be preferably employed in combination with the amylase-expressing yeast.

Transformation was performed based on the protocol outlined by Gietz et al., Nucl. Acid. Res., 20:1425 (1992). Transformed cells were then inoculated from agar into YEPD complex media broth (100 ml) and grown overnight at 30°C. The YEPD broth was prepared as described in Kaiser et al., Methods in Yeast Genetics, Cold Spring Harbor Press, Cold Spring Harbor, NY, p. 207 (1994). The overnight culture was then diluted to about 2×10^6 cells/ml (approx. OD₆₀₀=0.1) into fresh YEPD broth (500 ml) and regrown to 1×10^7 cells/ml (approx. OD₆₀₀=0.4-0.5).

The cells were then harvested and prepared for transformation by transfer into GS3 rotor bottles in a Sorval GS3 rotor at 5,000 rpm for 5 minutes, the supernatant discarded, and then resuspended into sterile water, and centrifuged again in 50 ml falcon tubes at 3,500 rpm in a Beckman GS-6KR centrifuge. The supernatant was discarded and the cells were subsequently washed with LiAc/TE (10 ml, 10 mM Tris-HCl, 1 mM EDTA pH 7.5, 100 mM Li₂OOCCH₃), and resuspended into LiAc/TE (2.5 ml).

Transformation took place by mixing the prepared cells (100 μ l) with freshly denatured single stranded salmon testes DNA (Lofstrand Labs, Gaithersburg, MD) and transforming DNA (1 μ g, vol. < 10 μ l) in microfuge tubes. The mixture was mixed briefly by vortexing, then 40% PEG/TE (600 μ l, 40% polyethylene glycol-4000, 10 mM Tris-HCl, 1 mM EDTA, 100 mM Li₂OOCCH₃, pH 7.5) was added. This mixture was gently mixed and incubated at 30°C while agitating for 30 minutes. The cells were then heat shocked at 42°C for 15 minutes, and the reaction vessel centrifuged in a microfuge at 12,000 rpm for 5-10 seconds, decanted and resuspended into TE (500 μ l, 10 mM Tris-HCl, 1 mM EDTA pH 7.5) followed by recentrifugation. The cells were then diluted into TE (1 ml) and aliquots (200 μ l) were spread onto the selective media previously prepared in 150 mm growth plates (VWR).

Alternatively, instead of multiple small reactions, the transformation was performed using a single, large scale reaction, wherein reagent amounts were scaled up accordingly.

The selective media used was a synthetic complete dextrose agar lacking uracil (SCD-Ura) prepared as described in Kaiser et al., Methods in Yeast Genetics, Cold Spring Harbor Press, Cold Spring Harbor, NY, p. 208-210 (1994). Transformants were grown at 30°C for 2-3 days.

The detection of colonies secreting amylase was performed by including red starch in the selective growth media. Starch was coupled to the red dye (Reactive Red-120, Sigma) as per the procedure described by Biely et al., Anal. Biochem., 172:176-179 (1988). The coupled starch was incorporated into the SCD-Ura agar plates at a final concentration of 0.15% (w/v), and was buffered with potassium phosphate to a pH of 7.0 (50-100 mM final concentration).

The positive colonies were picked and streaked across fresh selective media (onto 150 mm plates) in order to obtain well isolated and identifiable single colonies. Well isolated single colonies positive for amylase secretion were detected by direct incorporation of red starch into buffered SCD-Ura agar. Positive colonies were determined by their ability to break down starch resulting in a clear halo around the positive colony visualized directly.

25 4. Isolation of DNA by PCR Amplification

When a positive colony was isolated, a portion of it was picked by a toothpick and diluted into sterile water (30 μ l) in a 96 well plate. At this time, the positive colonies were either frozen and stored for subsequent analysis or immediately amplified. An aliquot of cells (5 μ l) was used as a template for the PCR reaction in a 25 μ l volume containing: 0.5 μ l KlenTaq (Clontech, Palo Alto, CA); 4.0 μ l 10 mM dNTP's (Perkin Elmer-Cetus); 2.5 μ l KlenTaq buffer (Clontech); 0.25 μ l forward oligo 1; 0.25 μ l reverse oligo 2; 12.5 μ l distilled water. The sequence of the forward oligonucleotide 1 was:

5'-TGTAACGACGCGCCAGTTAAATAGACCTGCAATTATTAATCT-3' (SEQ ID NO:3)

The sequence of reverse oligonucleotide 2 was:

5'-CAGGAAACAGCTATGACCACCTGCACACCTGCAAATCCATT-3' (SEQ ID NO:4)

35 PCR was then performed as follows:

- a. Denature 92°C, 5 minutes
- b. 3 cycles of: Denature 92°C, 30 seconds

| | | | | |
|----|----|---------------|-------|------------|
| | | Anneal | 59°C, | 30 seconds |
| | | Extend | 72°C, | 60 seconds |
| | c. | 3 cycles of: | | |
| | | Denature | 92°C, | 30 seconds |
| 5 | | Anneal | 57°C, | 30 seconds |
| | | Extend | 72°C, | 60 seconds |
| | d. | 25 cycles of: | | |
| | | Denature | 92°C, | 30 seconds |
| | | Anneal | 55°C, | 30 seconds |
| 10 | | Extend | 72°C, | 60 seconds |
| | e. | Hold | 4°C | |

The underlined regions of the oligonucleotides annealed to the ADH promoter region and the amylase region, respectively, and amplified a 307 bp region from vector pSST-AMY.0 when no insert was present. Typically, the first 18 nucleotides of the 5' end of these oligonucleotides contained annealing sites for the sequencing primers. Thus, the total product of the PCR reaction from an empty vector was 343 bp. However, signal sequence-fused cDNA resulted in considerably longer nucleotide sequences.

Following the PCR, an aliquot of the reaction (5 μ l) was examined by agarose gel electrophoresis in a 1% agarose gel using a Tris-Borate-EDTA (TBE) buffering system as described by Sambrook et al., *supra*. Clones resulting in a single strong PCR product larger than 400 bp were further analyzed by DNA sequencing after purification with a 96 Qiaquick PCR clean-up column (Qiagen Inc., Chatsworth, CA).

EXAMPLE 3: Isolation of cDNA Clones Using Signal Algorithm Analysis

Various polypeptide-encoding nucleic acid sequences were identified by applying a proprietary signal sequence finding algorithm developed by Genentech, Inc. (South San Francisco, CA) upon ESTs as well as clustered and assembled EST fragments from public (e.g., GenBank) and/or private (LIFESEQ®, Incyte Pharmaceuticals, Inc., Palo Alto, CA) databases. The signal sequence algorithm computes a secretion signal score based on the character of the DNA nucleotides surrounding the first and optionally the second methionine codon(s) (ATG) at the 5'-end of the sequence or sequence fragment under consideration. The nucleotides following the first ATG must code for at least 35 unambiguous amino acids without any stop codons. If the first ATG has the required amino acids, the second is not examined. If neither meets the requirement, the candidate sequence is not scored. In order to determine whether the EST sequence contains an authentic signal sequence, the DNA and corresponding amino acid sequences surrounding the ATG codon are scored using a set of seven sensors (evaluation parameters) known to be associated with secretion signals. Use of this algorithm resulted in the identification of numerous polypeptide-encoding nucleic acid sequences.

EXAMPLE 4: Isolation of cDNA clones Encoding Human PRO281

In order to obtain a cDNA clone encoding PRO281, methods described in Klein et al., *Proc. Natl. Acad. Sci. USA* 93:7108-7113 (1996) were employed with the following modifications. Yeast transformation was performed with limiting amounts of transforming DNA in order to reduce the number of multiple transformed yeast cells. Instead of plasmid isolation from the yeast followed by transformation of *E. coli* as

described in Klein et al., *supra*, PCR analysis was performed on single yeast colonies. PCR primers employed were bipartite in order to amplify the insert and a small portion of the invertase gene (allowing to determine that the insert was in frame with invertase) and to add on universal sequencing primer sites.

An invertase library was transformed into yeast and positives were selected on sucrose plates. Positive clones were re-tested and PCR products were sequenced. The sequence of one clone, PRO281, was determined to contain a signal peptide coding sequence. Oligonucleotide primers and probes were designed using the nucleotide sequence of PRO281. A full length plasmid library of cDNAs from human umbilical vein endothelium tissue was titrated and approximately 100,000 cfu were plated in 192 pools of 500 cfu/pool into 96-well round bottom plates. The plates were sealed and pools were grown overnight at 37°C with shaking (200rpm). PCR was performed on the individual cultures using primers. Agarose gel electrophoresis was performed and positive wells were identified by visualization of a band of the expected size. Individual positive clones were obtained by colony lift followed by hybridization with ³²P-labeled oligonucleotide. These clones were characterized by PCR, restriction digest, and southern blot analyses.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 80-82, and a stop signal at nucleotide positions 1115-1117 (Figure 1, SEQ ID NO:1). The predicted polypeptide precursor is 345 amino acids long, has a calculated molecular weight of approximately 37,205 daltons and an estimated pI of approximately 10.15. Analysis of the full-length PRO281 sequence shown in Figure 2 (SEQ ID NO:2) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 14, multiple transmembrane domains from about amino acid position 83 to about amino acid position 105, from about amino acid position 126 to about amino acid position 146, from about amino acid position 158 to about amino acid position 177, from about amino acid position 197 to about amino acid position 216, from about amino acid position 218 to about amino acid position 238, from about amino acid position 245 to about amino acid position 265, and from about amino acid position 271 to about amino acid position 290 and an amino acid sequence block having homology to G-protein coupled receptor proteins from about amino acid 115 to about amino acid 155. Clone UNQ244 (DNA16422-1209) has been deposited with ATCC on June 2, 1998 and is assigned ATCC deposit no. 209929.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 2 (SEQ ID NO:2), evidenced significant homology between the PRO281 amino acid sequence and the following Dayhoff sequences: H64634, AF033095_1, B64815, YBHL_ECOLI, EMEQUTR_1, AF064763_3, S53708, A69253, AF035413_12 and S63281.

EXAMPLE 5: Isolation of cDNA clones Encoding Human PRO276

In order to obtain a cDNA clone encoding PRO276, methods described in Klein et al., *PNAS*, 93:7108-7113 (1996) were employed with the following modifications. Yeast transformation was performed with limiting amounts of transforming DNA in order to reduce the number of multiple transformed yeast cells. Instead of plasmid isolation from the yeast followed by transformation of *E. coli* as described in Klein et al., *supra*, PCR analysis was performed on single yeast colonies. PCR primers employed were bipartite in order to amplify the

insert and a small portion of the invertase gene (allowing to determine that the insert was in frame with invertase) and to add on universal sequencing primer sites.

An invertase library was transformed into yeast and positives were selected on sucrose plates. Positive clones were re-tested and PCR products were sequenced. The sequence of one clone, PRO276, was determined to contain a signal peptide coding sequence. Oligonucleotide primers and probes were designed using the nucleotide sequence of PRO276. A full length plasmid library of cDNAs from human fetal liver cells was titrated and approximately 100,000 cfu were plated in 192 pools of 500 cfu/pool into 96-well round bottom plates. The plates were sealed and pools were grown overnight at 37 C with shaking (200rpm). PCR was performed on the individual cultures using primers. Agarose gel electrophoresis was performed and positive wells were identified by visualization of a band of the expected size. Individual positive clones were obtained by colony lift followed by hybridization with ³²P-labeled oligonucleotide. These clones were characterized by PCR, restriction digest, and southern blot analyses.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 180-182 and a stop signal at nucleotide positions 933-935 (Figure 3; SEQ ID NO:5). The predicted polypeptide precursor is 251 amino acids long has a calculated molecular weight of approximately 28,801 daltons and an estimated pI of approximately 9.58. The transmembrane domains are approximately at amino acids 98-116 and 152-172 of the sequence shown in Figure 4 (SEQ ID NO:6). Clone DNA16435-1208 (UNQ243) has been deposited with the ATCC and is assigned ATCC deposit no. 209930.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 4 (SEQ ID NO:6), revealed some sequence identity between the PRO276 amino acid sequence and the following Dayhoff sequences: CEG25D7_2, ATT8O5_2, S69696, GRHR_RAT, NPCBAABCD_3, AB013149_1, P_R85942 and AP000006_5.

EXAMPLE 6: Isolation of cDNA clones Encoding Human PRO189

A clone designated herein as DNA14187 was isolated as described in Example 2 above from a human retina tissue library. The DNA14187 sequence is shown in Figure 7 (SEQ ID NO:9). Based on the DNA14187 sequence shown in Figure 7 (SEQ ID NO:9), oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO189. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TTGACCTATACAGAGATTCATC-3' (SEQ ID NO:10); and
reverse PCR primer 5'-CTAAGAACTTCCCTCAGGATTTT-3' (SEQ ID NO:11).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA14187 sequence which had the following nucleotide sequence:

hybridization probe

5'-ATGAAGATCAATTTCAAGAAGCATGCACTTCTCCTCTTGC-3' (SEQ ID NO:12).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO189 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human retina tissue (LIB94). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO189 and the derived protein sequence for PRO189.

The entire nucleotide sequence of DNA21624-1391 is shown in Figure 5 (SEQ ID NO:7). Clone DNA21624-1391 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 200-202 and ending at the stop codon at nucleotide positions 1301-1303 (Figure 5). The predicted polypeptide precursor is 367 amino acids long (Figure 6). The full-length PRO189 protein shown in Figure 6 has an estimated molecular weight of about 41,871 daltons and a pI of about 5.06. Clone DNA21624-1391 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:8, the putative N-glycosylation sites are at about amino acids 224-227, 246-249 and 285-288. A domain for cytosolic fatty-acid binding proteins is at amino acids 78-107 of SEQ ID NO:8. The corresponding nucleotides can be routinely determined given the sequences provided herein.

Some sequence identity was found to W01A6.1 and F35D11.11, C. Elegans proteins, designated in a Dayhoff database as CEW01A6_10 and CELF35D11_11, respectively. Some sequence identity was also found to an antigen to malaria and to restin, designated in a Dayhoff database as P_R05766 and AF014012_1, respectively. Some sequence identity was also found to a microtubule binding protein and to myosin, designated in a Dayhoff database as AF041382_1 and S07537, respectively. There is also some sequence identity with 1-phosphatidylinositol-4, 5-bisphosphate, designated as PIP1_RAT.

EXAMPLE 7: Isolation of cDNA clones Encoding Human PRO190

A clone designated herein as DNA14232 was isolated as described in Example 2 above from a human fetal retina tissue library. The DNA14232 sequence is shown in Figure 10 (SEQ ID NO:15). Based on the DNA14232 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained

the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO190. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A
 5 positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTATACCTACTGTAGCTTCT-3' (SEQ ID NO:16); and

reverse PCR primer 5'-TCAGAGAATTCCTTCCAGGA-3' (SEQ ID NO:17).

10 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA14232 sequence which had the following nucleotide sequence:

hybridization probe

5'-ACAGTGCTGTAGTCATCCTGTAATATGCTCCTTGCAACA-3' (SEQ ID NO:18).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was
 15 screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO190 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human retina tissue (LIB94). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel
 20 electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave sequences which include the full-length
 25 DNA sequence for PRO190 [herein designated as DNA23334-1392] (SEQ ID NO:13) and the derived protein sequence for PRO190.

The entire nucleotide sequence of DNA23334-1392 is shown in Figure 8 (SEQ ID NO:13). Clone DNA23334-1392 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 193-195 and which ends at the stop codon at nucleotide positions 1465-1467 (Figure 8). The predicted
 30 polypeptide precursor is 424 amino acids long (Figure 9). The full-length PRO190 protein shown in Figure 9 has an estimated molecular weight of about 48,500 daltons and a pI of about 8.65. Clone DNA23334-1392 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:14, the putative transmembrane domains are at about
 35 amino acids 16-36, 50-74, 147-168, 229-250, 271-293, 298-318 and 328-368 of SEQ ID NO:14. N-glycosylation sites are at about amino acids 128-131, 204-207, 218-221 and 274-377 of SEQ ID NO:14. The corresponding nucleotides can be routinely determined given the sequences provided herein.

PRO190 has sequence identity with at least the following Dayhoff sequences designated as: CEZK896_2, JC5023, GMS1_SCHPO and S44668.

EXAMPLE 8: Isolation of cDNA clones Encoding Human PRO341

A clone designated herein as DNA12920 was isolated as described in Example 2 above from a human placenta tissue library. The DNA12920 sequence is shown in Figure 13 (SEQ ID NO:21). The DNA12920 sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., *Methods in Enzymology*, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence is herein designated DNA25314. Oligonucleotide primers based upon the DNA25314 sequence were then synthesized and employed to screen a human placenta cDNA library which resulted in the identification of the DNA26288-1239 clone shown in Figure 11. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 380-382, and a stop signal at nucleotide positions 1754-1756 (Figure 11, SEQ ID NO:19). The predicted polypeptide precursor is 458 amino acids long, has a calculated molecular weight of approximately 50,264 daltons and an estimated pI of approximately 8.17. Analysis of the full-length PRO341 sequence shown in Figure 12 (SEQ ID NO:20) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 17, transmembrane domains from about amino acid 171 to about amino acid 190, from about amino acid 220 to about amino acid 239, from about amino acid 259 to about amino acid 275, from about amino acid 286 to about amino acid 305, from about amino acid 316 to about amino acid 335, from about amino acid 353 to about amino acid 378 and from about amino acid 396 to about amino acid 417 and potential N-glycosylation sites from about amino acid 145 to about amino acid 147 and from about amino acid 155 to about amino acid 158. Clone DNA26288-1239 has been deposited with ATCC on April 21, 1998 and is assigned ATCC deposit no. 209792.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 12 (SEQ ID NO:20), evidenced homology between the PRO341 amino acid sequence and the following Dayhoff sequences: S75696, H69788, D69852, A69888, B64918, F64752, LPU89276_1, G64962, S52977 and S44253.

EXAMPLE 9: Isolation of cDNA clones Encoding Human PRO180

A clone designated herein as DNA12922 was isolated as described in Example 2 above from a human placenta tissue library. The DNA12922 sequence is shown in Figure 16 (SEQ ID NO:24). The DNA12922 sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a

proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., *Methods in Enzymology*, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

5 An oligonucleotide probe was formed based upon the consensus sequence obtained above. This probe had the following sequence.

5'-ACCTGTTAGAAATGTGGTGGTTTCAGCAAGGCCTCAGTTT (SEQ ID NO:25).

This probe was used to screen a human placenta library prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, 10 Holmes et al., *Science*, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp. A clone designated herein as DNA26843-1389 was obtained.

The entire nucleotide sequence of DNA26843-1389 is shown in Figure 14 (SEQ ID NO:22). Clone DNA26843-1389 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and ending at the stop codon at nucleotide positions 919-921 (Figure 14). The predicted 15 polypeptide precursor is 266 amino acids long (Figure 15). The full-length PRO180 protein shown in Figure 15 has an estimated molecular weight of about 29,766 daltons and a pI of about 8.39. Clone DNA26843-1389 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

20 Still analyzing the amino acid sequence of SEQ ID NO:23, the transmembrane domains are at about amino acids 13-33 (type II), 54-73, 94-113, 160-180 and 122-141 of SEQ ID NO:23. N-myristoylation sites are at about amino acids 57-62, 95-100, 99-104, 124-129 and 183-188 of SEQ ID NO:23. The corresponding nucleotides can be routinely determined given the sequences provided herein.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 15 (SEQ ID NO:23), evidenced some sequence 25 identity between the PRO180 amino acid sequence and the following Dayhoff sequences: CEC33A11_2, CEG11E6_5, CELW03A5_1 AND PEU83861_2 (NADH dehydrogenase subunit 4L, mitochondrion).

EXAMPLE 10: Isolation of cDNA clones Encoding Human PRO194

30 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein DNA19464. Based on the DNA19464 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO194. PCR primers (forward and reverse) were synthesized based upon the DNA19464 sequence. Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA19464 sequence.

35 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO194 gene using the probe oligonucleotide and one of the PCR primers. RNA

for construction of the cDNA libraries was isolated from human fetal lung tissue (LIB25).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO194 [herein designated as DNA26844-1394] (SEQ ID NO:27) and the derived protein sequence for PRO194.

The entire nucleotide sequence of DNA26844-1394 is shown in Figure 17 (SEQ ID NO:27). Clone
 5 DNA26844-1394 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 81-83 and ending at the stop codon at nucleotide positions 873-875 (Figure 17). The predicted polypeptide precursor is 264 amino acids long (Figure 18). The full-length PRO194 protein shown in Figure 18 has an estimated molecular weight of about 29,665 daltons and a pI of about 9.34. Analysis of the full-length PRO194 sequence shown in Figure 18 (SEQ ID NO:28) evidences the presence of various important
 10 polypeptides domains as shown in Figure 18. Clone DNA26844-1394 has been deposited with ATCC on June 2, 1998 and is assigned ATCC deposit no. 209926.

Analysis of the amino acid sequence of the full-length PRO194 polypeptide suggests that it does not exhibit significant sequence similarity to any known human protein. However, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some homology between the PRO194 amino acid sequence and
 15 the following Dayhoff sequences, HUMORFT_1, CET07F10_5, ATFCA9_12, F64934, YDIX_ECOLI, ATAF00065719F29G20.19, H70002, S76980, H64934 and S76385.

EXAMPLE 11: Isolation of cDNA clones Encoding Human PRO203

A clone designated herein as DNA15618 was isolated as described in Example 2 above from a human
 20 fetal lung tissue library. The DNA15618 sequence is shown in Figure 21 (SEQ ID NO:31). Oligonucleotide probes were generated from the sequence of the DNA15618 molecule and were used to screen a human fetal lung library (LIB26) prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

A full length clone was identified that contained a single open reading frame with an apparent
 25 translational initiation site at nucleotide positions 159-161 and ending at the stop codon found at nucleotide positions 1200-1202 (Figure 19; SEQ ID NO:29). The predicted polypeptide precursor is 347 amino acids long, has a calculated molecular weight of approximately 39,870 daltons and an estimated pI of approximately 6.76. Analysis of the full-length PRO203 sequence shown in Figure 20 (SEQ ID NO:30) evidences the presence of
 30 the following: a type II transmembrane domain at about amino acid 64 to about amino acid 87; possible N-glycosylation sites at about amino acid 147 to about amino acid 150, about amino acid 155 to about amino acid 158, and about amino acid 237 to about amino acid 240; sequence identity with heavy-metal-associated domain proteins at about amino acid 23 to about amino acid 45, and sequence identity with D-isomer specific 2-hydroxyacid dehydrogenase at about amino acid 24 to about amino acid 34. Clone DNA30862-1396 was
 35 deposited with the ATCC on June 2, 1998, and is assigned ATCC deposit no. 209920.

Analysis of the amino acid sequence of the full-length PRO203 polypeptide suggests that it possesses sequence similarity to GST ATPase, thereby indicating that PRO203 may be a novel GST ATPase. More

specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO203 amino acid sequence and the following Dayhoff sequences, AF008124_1, CFRCD1GEN_1, and P_R82566.

EXAMPLE 12: Isolation of cDNA clones Encoding Human PRO290

- 5 An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified that had homology to beige and FAN. An oligonucleotide probe based upon the identified EST sequence was then synthesized and used to screen human fetal kidney cDNA libraries in an attempt to identify a full-length cDNA clone. The oligonucleotide probe had the following sequence:
5' TGACTGCACTACCCCGTGGCAAGCTGTTGAGCCAGCTCAGCTG 3' (SEQ ID NO:34).
- 10 RNA for construction of cDNA libraries was isolated from human fetal kidney tissue. The cDNA libraries used to isolate the cDNA clones encoding human PRO290 were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as
- 15 pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science* 253:1278-1280 (1991)) in the unique XhoI and NotI.
- A cDNA clone was identified and sequenced in entirety. The entire nucleotide sequence of DNA35680-1212 is shown in Figure 22 (SEQ ID NO:32). Clone DNA35680-1212 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 293-295, and a stop codon at nucleotide positions
- 20 3302-3304 (Figure 22; SEQ ID NO:32). The predicted polypeptide precursor is 1003 amino acids long.
- It is currently believed that the PRO290 polypeptide is related to FAN and/or beige. Clone DNA35680-1212 has been deposited with ATCC and is assigned ATCC deposit no. 209790. It is understood that the deposited clone has the actual correct sequence rather than the representations provided herein. The full-length PRO290 protein shown in Figure 23 has an estimated molecular weight of about 112,013 daltons and a pI of
- 25 about 6.4.

EXAMPLE 13: Isolation of cDNA Clones Encoding Human PRO874

- A consensus DNA sequence designated herein as DNA36459 was identified using phrap as described in Example 1 above. Based on the DNA36459 consensus sequence, oligonucleotides were synthesized: 1) to
- 30 identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the coding sequence for PRO874.
- PCR primers (forward and reverse) were synthesized:
- forward PCR primer 5'-TCGTGCCCAGGGGCTGATGTGC-3' (SEQ ID NO:37); and
- reverse PCR primer 5'-GTCTTTACCCAGCCCCGGGATGCG-3' (SEQ ID NO:38).
- 35 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA36459 sequence which had the following nucleotide sequence:

hybridization probe

5'-GGCCTAATCCAACGTTCTGTCTTCAATCTGCAAATCTATGGGGTCCTGGG-3' (SEQ ID NO:39).

In order to screen several libraries for a source of a clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO874 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal lung tissue (LIB25).

DNA sequencing of the clones isolated as described above gave the DNA sequence for PRO874 [herein designated as DNA40621-1440] (SEQ ID NO:35) and the derived protein sequence for PRO874.

The entire nucleotide sequence of DNA40621-1440 is shown in Figure 24 (SEQ ID NO:35). Clone DNA40621-1440 contains a single open reading frame ending at the stop codon at nucleotide positions 964-966 (Figure 24). The predicted polypeptide encoded by DNA40621-1440 is 321 amino acids long (Figure 25). The PRO874 protein shown in Figure 25 has an estimated molecular weight of about 36,194 daltons and a pI of about 9.85. Analysis of the PRO874 sequence shown in Figure 25 (SEQ ID NO:36) evidenced the presence of the following: a type II transmembrane domain at about amino acids 57-80; additional transmembrane domains at about amino acids 110-126, 215-231, and 254-274; potential N-glycosylation sites at about amino acids 16-19, 27-30, and 289-292; sequence identity with hypothetical YBR002c family proteins at about amino acids 276-287; and sequence identity with ammonium transporter proteins at about amino acids 204-230. Clone DNA40621-1440 was deposited with the ATCC on June 2, 1998, and is assigned ATCC deposit no. 209922.

Analysis of the amino acid sequence of the PRO874 polypeptide suggests that it is a novel multi-span transmembrane protein. However, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO874 amino acid sequence and the following Dayhoff sequences: S67049, AF054839_1, S73437, S52460, and HIVU80570_1.

EXAMPLE 14: Isolation of cDNA Clones Encoding Human PRO710

A yeast screening assay was employed to identify cDNA clones that encoded potential secreted proteins. Use of this yeast screening assay allowed identification of a single cDNA clone whose sequence (herein designated as DNA38190) is shown in Figure 28 (SEQ ID NO:42). Based on the DNA38190 sequence shown in Figure 28, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO710. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TTCCGCAAAGAGTTCTACGAGGTGG-3' (SEQ ID NO:43)

reverse PCR primer 5'-ATTGACAACATTGACTGGCCTATGGG-3' (SEQ ID NO:44)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA38190 sequence which had the following nucleotide sequence

hybridization probe

5'-GTGGATGCTCTGTGTGCGTGCAAGATCCTTCAGGCCTTGTTCCAGTGTGA-3' (SEQ ID NO:45)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO710 gene using the probe oligonucleotide and one of the PCR primers.

- 5 RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

- 15 A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 67-69 and ending at the stop codon found at nucleotide positions 1765-1767 (Figure 26, SEQ ID NO:40). The predicted polypeptide precursor is 566 amino acids long, has a calculated molecular weight of approximately 65,555 daltons and an estimated pI of approximately 5.44. Analysis of the full-length PRO710 sequence shown in Figure 27 (SEQ ID NO:41) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 32, a transmembrane domain from about amino acid 454 to about amino acid 476, an aminoacyl-transfer RNA synthetase class-II signature sequence from about amino acid 6 to about amino acid 26 and potential N-glycosylation sites from about amino acid 111 to about amino acid 114, from about amino acid 146 to about amino acid 149 and from about amino acid 292 to about amino acid 295. Clone DNA44161-1434 has been deposited with ATCC on May 27, 1998 and is assigned ATCC deposit no. 209907.

- 25 Analysis of the amino acid sequence of the full-length PRO710 polypeptide suggests that it possesses significant sequence similarity to the CDC45 protein, thereby indicating that PRO710 may be a novel CDC45 homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO710 amino acid sequence and the following Dayhoff sequences, HSAJ3728_1, CEF34D10_1, S64939, UMUS0276_1, TRHY_SHEEP, CELT14E8_1, RNA1_YEAST, LVU89340_1, HSU80736_1 and CEZK337_2.

30 EXAMPLE 15: Isolation of cDNA clones Encoding Human PRO1151

- A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA40665. Based on the DNA40665 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1151.
- 35

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CCAGACGCTGCTCTTCGAAAGGGTC-3' (SEQ ID NO:48)

reverse PCR primer 5'-GGTCCCCGTAGGCCAGGTCCAGC-3' (SEQ ID NO:49)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40665 sequence which had the following nucleotide sequence

5 hybridization probe

5'-CTACTTCTTCAGCCTCAATGTGCACAGCTGGAATTACAAGGAGACGTACG-3' (SEQ ID NO:50)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1151 gene using the probe oligonucleotide and one of the PCR primers. RNA
10 for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1151 (designated herein as DNA44694-1500 [Figure 29, SEQ ID NO:46]; and the derived protein sequence for PRO1151.

The entire nucleotide sequence of DNA44694-1500 is shown in Figure 29 (SEQ ID NO:46). Clone
15 DNA44694-1500 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 272-274 and ending at the stop codon at nucleotide positions 1049-1051 (Figure 29). The predicted polypeptide precursor is 259 amino acids long (Figure 30). The full-length PRO1151 protein shown in Figure 30 has an estimated molecular weight of about 28,770 daltons and a pI of about 6.12. Analysis of the full-length PRO1151 sequence shown in Figure 30 (SEQ ID NO:47) evidences the presence of the following: a signal
20 peptide from about amino acid 1 to about amino acid 20, a potential N-glycosylation site from about amino acid 72 to about amino acid 75 and amino acid sequence blocks having homology to C1q domain-containing proteins from about amino acid 144 to about amino acid 178, from about amino acid 78 to about amino acid 111 and from about amino acid 84 to about amino acid 117. Clone UNQ581 (DNA44694-1500) has been deposited with ATCC on August 11, 1998 and is assigned ATCC deposit no. 203114.

25 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 30 (SEQ ID NO:47), evidenced significant homology between the PRO1151 amino acid sequence and the following Dayhoff sequences: ACR3_HUMAN, HP25_TAMAS, HUMC1QB2_1, P_R99306, CA1F_HUMAN, JX0369, CA24_HUMAN, S32436, P_R28916 and CA54_HUMAN.

30

EXAMPLE 16: Isolation of cDNA clones Encoding Human PRO1282

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein as DNA33778. Based on the DNA33778 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained
35 the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1282.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'TCTTCAGCCGCTTGCGCAACCTC3' (SEQ ID NO:53); and

reverse PCR primer 5'TTGCTCACATCCAGCTCCTGCAGG3' (SEQ ID NO:54).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA33778 sequence which had the following nucleotide sequence:

5 hybridization probe

5'TGGATGTTGTCCAGACAACCAGCTGGAGCTGTATCCGAGGC3' (SEQ ID NO:55).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1282 gene using the probe oligonucleotide and one of the PCR primers. RNA
10 for construction of the cDNA libraries was isolated from human fetal liver.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1282 (designated herein as DNA45495-1550 [Figure 31, SEQ ID NO:51]; and the derived protein sequence for PRO1282.

The entire coding sequence of PRO1282 is shown in Figure 31 (SEQ ID NO:51). Clone DNA45495-
15 1550 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 120-122, and an apparent stop codon at nucleotide positions 2139-2141 (SEQ ID NO:51). The predicted polypeptide precursor is 673 amino acids long. The signal peptide is at about amino acids 1-23; the transmembrane domain is at about amino acids 579-599; an EGF-like domain cysteine pattern signature starts at about amino acid 430; and leucine zipper patterns start at about amino acids 197 and 269 of SEQ ID NO:52,
20 see Figure 32. Clone DNA45495-1550 has been deposited with the ATCC and is assigned ATCC deposit no. 203156. The full-length PRO1282 protein shown in Figure 32 has an estimated molecular weight of about 71,655 daltons and a pI of about 7.8.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 32 (SEQ ID NO:52), revealed sequence identity
25 between the PRO1282 amino acid sequence and the following Dayhoff sequences (data from database incorporated by reference): AB007876_1, RNPLGPV_1, MUSLRRP_1, ALS_PAPPA, AC004142_1, ALS_HUMAN, AB014462_1, DMTARTAN_1, HSCHON03_1 and S46224.

EXAMPLE 17: Isolation of cDNA clones Encoding Human PRO358

30 Using the method described in Example 1 above, a single EST sequence was identified in the Incyte database, designated herein as INC3115949. Based on the INC3115949 EST sequence, oligonucleotides were synthesized to identify by PCR a cDNA library that contained the sequence of interest and for use as probes to isolate a clone of the full-length coding sequence for PRO358.

A pair of PCR primers (forward and reverse) were synthesized:

35 forward PCR primer 5'-TCCCACCAGGTATCATAAACTGAA-3' (SEQ ID NO:58)

reverse PCR primer 5'-TTATAGACAATCTGTTCTCATCAGAGA-3' (SEQ ID NO:59)

A probe was also synthesized:

5'-AAAAAGCATACTTGGGAATGGCCCAAGGATAGGTGTAATG-3' (SEQ ID NO:60)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO358 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human bone marrow (LIB256). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO358 (Figure 33, SEQ ID NO:56) and the derived protein sequence for PRO358 (Figures 34, SEQ ID NO:57).

The entire nucleotide sequence of the clone identified (DNA47361-1154) is shown in Figure 33 (SEQ ID NO:56). Clone DNA47361-1154 contains a single open reading frame with an apparent translational initiation site (ATG start signal) at nucleotide positions underlined in Figure 33. The predicted polypeptide precursor is 811 amino acids long, including a putative signal sequence (amino acids 1 to 19), an extracellular domain (amino acids 20 to 575, including leucine rich repeats in the region from position 55 to position 575), a putative transmembrane domain (amino acids 576 to 595). Clone DNA47361-1249 has been deposited with ATCC and is assigned ATCC deposit no. 209431.

EXAMPLE 18: Isolation of cDNA clones Encoding Human PRO1310

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein as DNA37164. Based on the DNA37164 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1310.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'GTTCTCAATGAGCTACCCGTCCCC3' (SEQ ID NO:63) and
reverse PCR primer: 5'CGCGATGTAGTGGAACCTCGGGCTC3' (SEQ ID NO:64).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47394 sequence which had the following nucleotide sequence:

hybridization probe:

5'ATCCGCATAAACCCCTCAGTCCTGGTTTGATAATGGGAGCATCTGCATGAG3' (SEQ ID NO:65).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to

isolate clones encoding the PRO1310 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1310 and the derived protein sequence for PRO1310.

The entire coding sequence of PRO1310 is shown in Figures 35A-B (SEQ ID NO:61). Clone
 5 DNA47394-1572 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 326-328, and an apparent stop codon at nucleotide positions 2594-2596 (SEQ ID NO:61). The predicted polypeptide precursor is 765 amino acids long. The signal peptide is at about amino acids 1-25 of SEQ ID NO:62. Clone DNA47394-1572 has been deposited with ATCC and is assigned ATCC deposit no. 203109. The full-length PRO1310 protein shown in Figure 36 has an estimated molecular weight of about 85,898 daltons
 10 and a pI of about 6.87.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 36 (SEQ ID NO:62), revealed sequence identity between the PRO1310 amino acid sequence and the following Dayhoff sequences: AF017639_1, P_W36817, JC5256, CBPH_HUMAN, MMU23184_1, CBPN_HUMAN, HSU83411_1, CEF01D4_7, RNU62897_1 and
 15 P_W11851.

EXAMPLE 19: Isolation of cDNA Clones Encoding Human PRO698

A yeast screening assay was employed to identify cDNA clones that encoded potential secreted proteins. Use of this yeast screening assay allowed identification of a single cDNA clone whose sequence (herein
 20 designated as DNA39906) is shown in Figure 39 (SEQ ID NO:68). Based on the DNA39906 sequence shown in Figure 39, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO698. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A
 25 positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-AGCTGTGGTCATGGTGGTGTGGTG-3' (SEQ ID NO:69)

reverse PCR primer 5'-CTACCTTGGCCATAGGTGATCCGC-3' (SEQ ID NO:70)

30 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA39906 sequence which had the following nucleotide sequence

hybridization probe

5'-CATCAGCAAACCGTCTGTGGTTCAGCTCAACTGGAGAGGGTT-3' (SEQ ID NO:71)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was
 35 screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO698 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human bone marrow tissue (LIB255). The cDNA

libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 14-16 and ending at the stop codon found at nucleotide positions 1544-1546 (Figure 37, SEQ ID NO:66). The predicted polypeptide precursor is 510 amino acids long, has a calculated molecular weight of approximately 57,280 daltons and an estimated pI of approximately 5.61.

Analysis of the full-length PRO698 sequence shown in Figure 38 (SEQ ID NO:67) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 20, potential N-glycosylation sites from about amino acid 72 to about amino acid 75, from about amino acid 136 to about amino acid 139, from about amino acid 193 to about amino acid 196, from about amino acid 253 to about amino acid 256, from about amino acid 352 to about amino acid 355 and from about amino acid 411 to about amino acid 414 an amino acid block having homology to legume lectin beta-chain proteins from about amino acid 20 to about amino acid 39 and an amino acid block having homology to the HBGF/FGF family of proteins from about amino acid 338 to about amino acid 365. Clone DNA48320-1433 has been deposited with ATCC on May 27, 1998 and is assigned ATCC deposit no. 209904.

Analysis of the amino acid sequence of the full-length PRO698 polypeptide suggests that it possesses significant sequence similarity to the olfactomedin protein, thereby indicating that PRO698 may be a novel olfactomedin homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO698 amino acid sequence and the following Dayhoff sequences, OLFM_RANCA, I73637, AB006686S3_1, RNU78105_1, RNU72487_1, P_R98225, CELC48E7_4, CEF11C3_3, XLU85970_1 and S42257.

EXAMPLE 20: Isolation of cDNA Clones Encoding Human PRO732

A yeast screening assay was employed to identify cDNA clones that encoded potential secreted proteins. Use of this yeast screening assay allowed identification of a single cDNA clone whose sequence (herein designated as DNA42580) is shown in Figure 45 (SEQ ID NO:77). The DNA42580 sequence was then compared to a variety of known EST sequences to identify homologies. The EST databases employed included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)) as a comparison to a 6 frame translation of the EST sequence. Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

Using the above analysis, a consensus DNA sequence was assembled relative to other EST sequences using phrap. This consensus sequence is herein designated consen01. Proprietary Genentech EST sequences were employed in the consensus assembly and they are herein designated DNA20239 (Figure 42; SEQ ID NO:74), DNA38050 (Figure 43; SEQ ID NO:75) and DNA40683 (Figure 44; SEQ ID NO:76).

Based on the consen01 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO732. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-ATGTTTGTGTGGAAGTGCCCG-3' (SEQ ID NO:78)

forward PCR primer 5'-GTCAACATGCTCCTCTGC-3' (SEQ ID NO:79)

reverse PCR primer 5'-AATCCATTGTGCACTGCAGCTCTAGG-3' (SEQ ID NO:80)

reverse PCR primer 5'-GAGCATGCCACCACTGGACTGAC-3' (SEQ ID NO:81)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA44143 sequence which had the following nucleotide sequence

hybridization probe

5'-GCCGATGCTGCTCCTAGTGGAACAACCTCCACTGTAAGTAGATTGATCTATGCAC-3' (SEQ ID NO:82)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO732 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human fetal lung tissue (LIB26). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 88-90 and ending at the stop codon found at nucleotide positions 1447-1449 (Figure 40, SEQ ID NO:72). The predicted polypeptide precursor is 453 amino acids long, has a calculated molecular weight of approximately 50,419 daltons and an estimated pI of approximately 5.78. Analysis of the full-length PRO732 sequence shown in Figure 41 (SEQ ID NO:73) evidences the presence of

the following: a signal peptide from about amino acid 1 to about amino acid 28, transmembrane domains from about amino acid 37 to about amino acid 57, from about amino acid 93 to about amino acid 109, from about amino acid 126 to about amino acid 148, from about amino acid 151 to about amino acid 172, from about amino acid 197 to about amino acid 215, from about amino acid 231 to about amino acid 245, from about amino acid 260 to about amino acid 279, from about amino acid 315 to about amino acid 333, from about amino acid 384 to about amino acid 403 and from about amino acid 422 to about amino acid 447, potential N-glycosylation sites from about amino acid 33 to about amino acid 36, from about amino acid 34 to about amino acid 37, from about amino acid 179 to about amino acid 183, from about amino acid 298 to about amino acid 301, from about amino acid 337 to about amino acid 340 and from about amino acid 406 to about amino acid 409, an amino acid block having homology to the MIP family of proteins from about amino acid 119 to about amino acid 149 and an amino acid block having homology to DNA/RNA non-specific endonuclease proteins from about amino acid 279 to about amino acid 286. Clone DNA48334-1435 has been deposited with ATCC on June 2, 1998 and is assigned ATCC deposit no. 209924.

Analysis of the amino acid sequence of the full-length PRO732 polypeptide suggests that it possesses significant sequence similarity to the Diff33 protein, thereby indicating that PRO732 may be a novel Diff33 homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO732 amino acid sequence and the following Dayhoff sequences, HS179M20_2, MUSTETU_1, CER11H6_2, RATDRP_1, S51256, E69226, AE000869_1, JC4120, CYB_PARTE and P_R50619.

20 EXAMPLE 21: Isolation of cDNA clones Encoding Human PRO1120

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein consen0352. The consen0352 sequence was then extended using repeated cycles of BLAST and phrap to extend the consensus sequence as far as possible using the sources of EST sequences discussed above. The extended consensus sequence is designated herein as DNA34365. Based on the DNA34365 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1120.

PCR primers (forward and reverse) were synthesized:

forward PCR primers: 5'-GAAGCCGGCTGTCTGAATC-3' (SEQ ID NO:85),
 30 5'-GGCCAGCTATCTCCGAG-3' (SEQ ID NO:86), 5'-AAGGGCCTGCAAGAGAAG-3' (SEQ ID NO:87),
 5'-CACTGGGACAACTGTGGG-3' (SEQ ID NO:88),
 5'-CAGAGGCAACGTGGAGAG-3' (SEQ ID NO:89), and
 5'-AAGTATTGTCATACAGTGTTTC-3' (SEQ ID NO:90);
reverse PCR primers: 5'-TAGTACTTGGGCACGAGTTGGAG-3' (SEQ ID NO:91), and 5'-
 35 TCATACCAACTGCTGGTCATTGGC-3' (SEQ ID NO:92).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA34365 consensus sequence which had the following nucleotide sequence:

hybridization probe:

5'-CTCAAGCTGCTGGACACGGAGCGGCCGGTGAATCGGTTTCACTTG-3' (SEQ ID NO:93).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO1120 gene using the probe oligonucleotide and one of the PCR primers. RNA
5 for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1120 (designated herein as DNA48606-1479 [Figures 46A-B, SEQ ID NO:83]; and the derived protein sequence for PRO1120.

The entire coding sequence of PRO1120 is shown in Figures 46A-B (SEQ ID NO:83). Clone
10 DNA48606-1479 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 608-610 and an apparent stop codon at nucleotide positions 3209-3211. The predicted polypeptide precursor is 867 amino acids long. The full-length PRO1120 protein shown in Figure 47 has an estimated molecular weight of about 100,156 Daltons and a pI of about 9.44. Additional features of the PRO1120 polypeptide include a signal peptide at about amino acids 1-17; a sulfatase signature at about amino acids 86-98;
15 regions of homology to sulfatases at about amino acids 87-106, 133-146, 216-229, 291-320, and 365-375; and potential N-glycosylation sites at about amino acids 65-68, 112-115, 132-135, 149-152, 171-174, 198-201, 241-245, 561-564, 608-611, 717-720, 754-757, and 764-767.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 47 (SEQ ID NO:84), revealed significant
20 homology between the PRO1120 amino acid sequence and the following Dayhoff sequences: CELK09C4_1, GL6S_HUMAN, G65169, NCU89492_1, BCU44852_1, E64903, P_R51355, STS_HUMAN, GA6S_HUMAN, and IDS_MOUSE. Clone DNA48606-1479 was deposited with the ATCC on July 1, 1998, and is assigned ATCC deposit no. 203040.

25 EXAMPLE 22: Isolation of cDNA clones Encoding Human PRO537

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated as Incyte EST cluster no. 29605. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto,
30 CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA48350.

35 In light of an observed sequence homology between the DNA48350 consensus sequence and an EST sequence encompassed within the Merck EST clone no. R63443, the Merck EST clone R63443 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.

The sequence of this cDNA insert is shown in Figure 48 and is herein designated as DNA49141-1431.

Clone DNA49141-1431 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 97-99 and ending at the stop codon at nucleotide positions 442-444 (Figure 48). The predicted polypeptide precursor is 115 amino acids long (Figure 49). The full-length PRO537 protein shown in Figure 49 has an estimated molecular weight of about 13,183 daltons and a pI of about 12.13. Analysis of the full-length PRO537 sequence shown in Figure 49 (SEQ ID NO:95) evidences the presence of the following:

5 a signal peptide from about amino acid 1 to about amino acid 31, a potential N-glycosylation site from about amino acid 44 to about amino acid 47, potential N-myristoylation sites from about amino acid 3 to about amino acid 8 and from about amino acid 16 to about amino acid 21 and an amino acid block having homology to multicopper oxidase proteins from about amino acid 97 to about amino acid 105. Clone DNA49141-1431 has

10 been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203003.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 49 (SEQ ID NO:95), evidenced homology between the PRO537 amino acid sequence and the following Dayhoff sequences: A54523, CELF22H10_2, FK44_MOUSE, OTX1_HUMAN, URB1_USTMA, KNOB_PLAFN, A32895_1, AF036332_1, HRG_HUMAN

15 and HRP3_PLAFS.

EXAMPLE 23: Isolation of cDNA clones Encoding Human PRO536

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated herein as ss.clu2437.init. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ[®], Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA48351.

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In light of an observed sequence homology between the DNA48351 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H11129, the Merck EST clone H11129 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.

30 The sequence of this cDNA insert is shown in Figure 50 and is herein designated as DNA49142-1430.

Clone DNA49142-1430 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 48-50 and ending at the stop codon at nucleotide positions 987-989 (Figure 50). The predicted polypeptide precursor is 313 amino acids long (Figure 51). The full-length PRO536 protein shown in Figure 51 has an estimated molecular weight of about 34,189 daltons and a pI of about 4.8. Analysis of the full-length PRO536 sequence shown in Figure 51 (SEQ ID NO:97) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25, a potential N-glycosylation site from about amino acid 45 to about amino acid 48 and an amino acid sequence block having homology to sulfatase proteins from

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about amino acid 16 to about amino acid 26. Clone DNA49142-1430 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203002.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 51 (SEQ ID NO:97), evidenced homology between the PRO536 amino acid sequence and the following Dayhoff sequences: APU46857_1, PK2_DICDI,
 5 H64743, F5I14_18, CEAM_ECOLI, GEN14267, H64965, TCU39815_1, PSBJ_ODOSI and P_R06980.

EXAMPLE 24: Isolation of cDNA clones Encoding Human PRO535

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated herein as ss.clu12694.init. This EST cluster sequence was
 10 then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and
 15 assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA48352. Two proprietary Genentech EST sequences were employed in the assembly are herein shown in Figures 54 and 55.

In light of an observed sequence homology between the DNA48352 consensus sequence and an EST
 20 sequence encompassed within the Merck EST clone no. H86994, the Merck EST clone H86994 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 52 and is herein designated as DNA49143-1429.

Clone DNA49143-1429 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 78-80 and ending at the stop codon at nucleotide positions 681-683 (Figure 52). The
 25 predicted polypeptide precursor is 201 amino acids long (Figure 53). The full-length PRO535 protein shown in Figure 53 has an estimated molecular weight of about 22,180 daltons and a pI of about 9.68. Analysis of the full-length PRO535 sequence shown in Figure 53 (SEQ ID NO:99) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25, a transmembrane domain from about amino acid 155 to about amino acid 174, a potential N-glycosylation site from about amino acid 196 to about amino acid
 30 199 and FKBP-type peptidyl-prolyl cis-trans isomer signature sequences from about amino acid 62 to about amino acid 77, from about amino acid 87 to about amino acid 123 and from about amino acid 128 to about amino acid 141. Clone DNA49143-1429 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203013.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST- sequence
 35 alignment analysis of the full-length sequence shown in Figure 53 (SEQ ID NO:99), evidenced homology between the PRO535 amino acid sequence and the following Dayhoff sequences: S71237, P_R93551, P_R28980, S71238, FKB2_HUMAN, CELC05C8_1, S55383, S72485, CELC50F2_6 and S75144.

EXAMPLE 25: Isolation of cDNA clones Encoding Human PRO718

A cDNA sequence isolated in the amylase screen described in Example 2 (human fetal lung library) above is herein designated DNA43512 (see Figure 62; SEQ ID NO:108). The DNA43512 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to
 5 identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA45625. Proprietary
 10 Genentech EST sequences were employed in the assembly and are herein shown in Figures 58-61.

Based on the DNA45625 sequence, oligonucleotide probes were generated and used to screen a human fetal lung library (LIB25) prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

15 PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GGGTGGATGGTACTGCTGCATCC-3' (SEQ ID NO:109)

reverse PCR primer 5'-TGTTGTGCTGTGGGAAATCAGATGTG-3' (SEQ ID NO:110)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA45625 sequence which had the following nucleotide sequence:

20 hybridization probe

5'-GTGTCTGGAGGCTGTGGCCGTTTGTCTTGGGCTAAAATCGGG-3' (SEQ ID NO:111)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO718 gene using the probe oligonucleotide and one of the PCR primers.

25 A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 36-38 and ending at the stop codon found at nucleotide positions 607-609 (Figure 56; SEQ ID NO:102). The predicted polypeptide precursor is 157 amino acids long, has a calculated molecular weight of approximately 17,400 daltons and an estimated pI of approximately 5.78. Analysis of the full-length PRO718 sequence shown in Figure 57 (SEQ ID NO:103) evidences the presence of
 30 the following: a type II transmembrane domain from about amino acid 21 to about amino acid 40, and other transmembrane domains at about amino acid 58 to about amino acid 78, about amino acid 95 to about amino acid 114, and about amino acid 127 to about amino acid 147; a cell attachment sequence from about amino acid 79 to about amino acid 81; and a potential N-glycosylation site from about amino acid 53 to about amino acid 56. Clone DNA49647-1398 has been deposited with ATCC on June 2, 1998 and is assigned ATCC deposit no.
 35 209919.

Analysis of the amino acid sequence of the full-length PRO718 polypeptide suggests that it possesses no significant sequence similarity to any known protein. However, an analysis of the Dayhoff database (version

35.45 SwissProt 35) evidenced some degree of homology between the PRO718 amino acid sequence and the following Dayhoff sequences: AF045606_1, AF039906_1, SPBC8D2_2, S63441, F64728, COX1_TRYBB, F64375, E64173, RPYGJT_3, MTCY261_23.

EXAMPLE 26: Isolation of cDNA clones Encoding Human PRO872

5 Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence designated herein as clu120709.init. The clu120709.init sequence was then compared a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology, 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or
10 in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA48254.

In light of an observed sequence homology between the DNA48254 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3438068, the Incyte EST clone 3438068 was purchased
15 and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 63 and is the full-length DNA sequence for PRO872. Clone DNA49819-1439 was deposited with the ATCC on June 2, 1998, and is assigned ATCC deposit no. 209931.

The entire nucleotide sequence of DNA49819-1439 is shown in Figure 63 (SEQ ID NO:112). Clone
20 DNA49819-1439 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 14-16 and ending at the stop codon at nucleotide positions 1844-1846 (Figure 63). The predicted polypeptide precursor is 610 amino acids long (Figure 64). The full-length PRO872 protein shown in Figure 64 has an estimated molecular weight of about 66,820 daltons and a pI of about 8.65. Analysis of the full-length PRO872 sequence shown in Figure 64 (SEQ ID NO:113) evidences the presence of the following features: a
25 signal peptide at amino acid 1 to about 18, putative transmembrane domains at about amino acids 70-87, 200-222 and 568-588; sequence identity with bacterial-type phytoene dehydrogenase protein at about amino acids 71-105; sequence identity with a regulator of chromosome condensation (RCC1) signature 2 at about amino acids 201-211; leucine zipper patterns at about amino acids 214-235, 221-242, 228-249 and 364-385; a potential N-glycosylation site at about amino acids 271-274; and a glycosaminoglycan attachment site at about amino acids
30 75-78. Analysis of the amino acid sequence of the full-length PRO872 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO872 amino acid sequence and the following Dayhoff sequences: PRCRT1_1, S75951, S74689, CELF37C4_3, CRT1_RHOCA, S76617, YNI2_METTL, MTV014_14, AOFB_HUMAN, and MMU70429_1.

EXAMPLE 27: Isolation of cDNA clones Encoding Human PRO1063

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence designated herein as ss.clu119743.init. The Incyte EST cluster sequence

ss.clu119743.init sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA48288.

In light of an observed sequence homology between the DNA48288 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2783726, the Incyte EST clone 2783726 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 65 and is herein designated DNA49820-1427.

The full length clone shown in Figure 65 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 90-92 and ending at the stop codon found at nucleotide positions 993-995 (Figure 65; SEQ ID NO:114). The predicted polypeptide precursor is 301 amino acids long, has a calculated molecular weight of approximately 33,530 daltons and an estimated pI of approximately 4.80. Analysis of the full-length PRO1063 sequence shown in Figure 66 (SEQ ID NO:115) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 21, potential N-glycosylation sites from about amino acid 195 to about amino acid 198, from about amino acid 217 to about amino acid 220 and from about amino acid 272 to about amino acid 275, a glycosaminoglycan attachment site from about amino acid 267 to about amino acid 270, a microbodies C-terminal targeting signal site from about amino acid 299 to about amino acid 301, a type II fibronectin collagen-binding domain homology sequence from about amino acid 127 to about amino acid 168 and a fructose-bisphosphate aldolase class II protein homology sequence from about amino acid 101 to about amino acid 118. Clone DNA49820-1427 has been deposited with the ATCC on June 2, 1998 and is assigned ATCC deposit no. 209932.

Analysis of the amino acid sequence of the full-length PRO1063 polypeptide suggests that it possesses sequence similarity to the human type IV collagenase protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO1063 amino acid sequence and the following Dayhoff sequences, S68303, CFU68533_1, P_P91139, RNU65656_1, PA2R_RABIT, MMU56734_1, FINC_XENLA, A48925, P_R92778 and FA12_HUMAN.

EXAMPLE 28: Isolation of cDNA clones Encoding Human PRO619

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated herein as 88434. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score

of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1656694, the Incyte EST clone 1656694 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 67 and is herein designated as DNA49821-1562.

The full length clone shown in Figure 67 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 81-83 and ending at the stop codon found at nucleotide positions 450-452 (Figure 67; SEQ ID NO:116). The predicted polypeptide precursor (Figure 68, SEQ ID NO:117) is 123 amino acids long including a predicted signal peptide at about amino acids 1-20. PRO619 has a calculated molecular weight of approximately 13,710 daltons and an estimated pI of approximately 5.19. Clone DNA49821-1562 was deposited with the ATCC on June 16, 1998 and is assigned ATCC deposit no. 209981.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 68 (SEQ ID NO:117), revealed significant homology between the PRO619 amino acid sequence and the following Dayhoff sequences: S35302, D87009_1, HSU93494_1, HUMIGLAM5_1, D86999_2, HUMIGLYM1_1, HUMIGLYMKE_1, A29491_1, A29498_1, and VPR2_MOUSE.

EXAMPLE 29: Isolation of cDNA clones Encoding Human PRO943

A consensus DNA sequence encoding PRO943 was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence was then extended using repeated cycles of BLAST and phrap to extend the consensus sequence as far as possible using the sources of EST sequences discussed above. The extended consensus sequence is herein designated DNA36360. Based on the DNA36360 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO943.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CGAGATGACGCCGAGCCCC-3' (SEQ ID NO:120)

reverse PCR primer 5'-CGGTTTCGACACGCGGCAGGTG-3' (SEQ ID NO:121)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA36360 sequence which had the following nucleotide sequence

hybridization probe

5'-TGCTGCTCCTGCTGCCGCCGCTGCTGCTGGGGCCCTCCCGCCGG-3' (SEQ ID NO:122)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO943 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal brain tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO943 (designated herein as DNA52192-1369 [Figure 69, SEQ ID NO:118]) and the derived protein sequence for PRO943.

The entire nucleotide sequence of DNA52192-1369 is shown in Figure 69 (SEQ ID NO:118). Clone DNA52192-1369 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 150-152 and ending at the stop codon at nucleotide positions 1662-1664 (Figure 69). The predicted polypeptide precursor is 504 amino acids long (Figure 70). The full-length PRO943 protein shown in Figure 70 has an estimated molecular weight of about 54,537 daltons and a pI of about 10.04. Analysis of the full-length PRO943 sequence shown in Figure 70 (SEQ ID NO:119) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 17, a transmembrane domain from about amino acid 376 to about amino acid 396, tyrosine kinase phosphorylation sites from about amino acid 212 to about amino acid 219 and from about amino acid 329 to about amino acid 336, potential N-glycosylation sites from about amino acid 111 to about amino acid 114, from about amino acid 231 to about amino acid 234, from about amino acid 255 to about amino acid 258 and from about amino acid 293 to about amino acid 296 and an immunoglobulin and MHC protein sequence homology block from about amino acid 219 to about amino acid 236. Clone DNA52192-1369 has been deposited with ATCC on July 1, 1998 and is assigned ATCC deposit no. 203042.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 70 (SEQ ID NO:119), evidenced significant homology between the PRO943 amino acid sequence and the following Dayhoff sequences: B49151, A39752, FGR1_XENLA, S38579, RATHBFGFRB_1, TVHU2F, FGR2_MOUSE, CEK3_CHICK, P_R21080 and A27171_1.

EXAMPLE 30: Isolation of cDNA clones Encoding Human PRO1188

A consensus DNA sequence was assembled relative to other EST sequences using the program "phrap" as described in Example 1 above. This consensus sequence is designated herein as DNA45679. Based on the DNA45679 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1188.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTGGTGCCTCAACAGGGAGCAG-3' (SEQ ID NO:125)
reverse PCR primer 5'-CCATTGTGCAGGTCAGGTCACAG-3' (SEQ ID NO:126)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA45679 sequence which had the following nucleotide sequence:

hybridization probe

5'-CTGGAGCAAGTGCTCAGCTGCCTGTGGTCAGACTGGGGTC-3' (SEQ ID NO:127)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1188 gene using the probe oligonucleotide and one of the PCR primers. RNA

for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1188 (designated herein as DNA52598-1518 [Figure 71, SEQ ID NO:123]); and the derived protein sequence for: PRO1188.

The entire coding sequence of PRO1188 is shown in Figure 71 (SEQ ID NO:123). Clone DNA52598-1518 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 136-138 and an apparent stop codon at nucleotide positions 3688-3690. The predicted polypeptide precursor is 1184 amino acids long. The full-length PRO1188 protein shown in Figure 72 has an estimated molecular weight of about 132,582 Daltons and a pI of about 8.80. Additional features include: a signal peptide at about amino acids 1-31; an ATP/GTP binding site motif A (P-loop) at about amino acids 266-273; an aldehyde dehydrogenases cysteine active site at about amino acids 188-199; growth factor and cytokines receptors family signature 2 at about amino acids 153-159; and potential N-glycosylation sites at about amino acids 129-132, 132-135, 346-349, 420-423, 550-553, 631-634, 1000-1003, and 1056-1059.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 72 (SEQ ID NO:124), revealed significant homology between the PRO1188 amino acid sequence and the following Dayhoff sequences: SSU83114_1, S56015, CET21B6_4, CELT19D2_1, and TSP1_MOUSE.

Clone DNA52598-1518 has been deposited with ATCC and is assigned ATCC deposit no 203107.

EXAMPLE 31: Isolation of cDNA clones Encoding Human PRO1133

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This sequence was extended using repeated cycles of phrap. The extended consensus sequence is designated herein DNA38102. Based on the DNA38102 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1133.

PCR primers (two forward and one reverse) were synthesized:

forward PCR primer 1 5'-TCGATTATGGACGAACATGGCAGC-3' (SEQ ID NO:130);

forward PCR primer 2 5'-TTCTGAGATCCCTCATCCTC-3' (SEQ ID NO:131); and

reverse primer 5'-AGGTTTCAGGGACAGCAAGTTTGGG-3' (SEQ ID NO:132).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA38102 sequence which had the following nucleotide sequence:

hybridization probe

5'TTTGCTGGACCTCGGCTACGGAATTGGCTTCCTCTACGGACAGCTGGAT3' (SEQ ID NO:133).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with a PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1133 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1133 and the derived protein sequence for PRO1133.

The entire coding sequence of PRO1133 is shown in Figure 73 (SEQ ID NO:128). Clone DNA53913-1490 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 266-268 and an apparent stop codon at nucleotide positions 1580-1582 of SEQ ID NO:128. The predicted polypeptide precursor is 438 amino acids long. The signal peptide is at amino acids 1-18 of SEQ ID NO:129. EGF-like domain cysteine pattern signatures start at 315 and 385 of SEQ ID NO:129 as shown in Figure 74. Clone DNA53913-1490 has been deposited with ATCC and is assigned ATCC deposit no. 203162. The full-length PRO1133 protein shown in Figure 74 has an estimated molecular weight of about 49,260 daltons and a pI of about 6.15.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 74 (SEQ ID NO:129), revealed some sequence identity between the PRO1133 amino acid sequence and the following Dayhoff sequences (data from the database incorporated herein): AF002717_1, LMG1_HUMAN, B54665, UNC6_CAEEL, LML1_CAEEL, LMA5_MOUSE, MMU88353_1, LMA1_HUMAN, HSLN2C64_1 and AF005258_1.

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EXAMPLE 32: Isolation of cDNA clones Encoding Human PRO784

An initial DNA sequence (SEQ ID NO:136), referred to herein as DNA44661 and shown in Figure 77, was identified using a yeast screen, in a human fetal lung cDNA library that preferentially represents the 5' ends of the primary cDNA clones. DNA44661 was then compared to ESTs from public databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA), using the computer program BLAST or BLAST2 [Altschul et al., *Methods in Enzymology*, 266:460-480 (1996)]. The ESTs were then clustered and assembled into a consensus DNA sequence using the computer program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained is designated herein as "DNA45463". Based on the DNA45463 consensus sequence, oligonucleotides were synthesized for use as probes to isolate a clone of the full-length coding sequence for PRO784 from a human fetal lung cDNA library.

The full length DNA53978-1443 clone shown in Figure 75 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 37-39 and ending at the stop codon found at nucleotide positions 821-823 (Figure 75; SEQ ID NO:134). The predicted polypeptide precursor (Figure 76, SEQ ID NO:135) is 228 amino acids long. PRO784 has a calculated molecular weight of approximately 25,735 Daltons and an estimated pI of approximately 5.45. PRO784 has the following features: a signal peptide at about amino acid 1 to about 15; transmembrane domains at about amino acids 68 to about 87 and at about 183 to about 204; potential N-myristoylation sites at about amino acids 15-20, 51-56, 66-60, 163-168, and 206-211; and an RNP-1 protein RNA-binding region at about amino acids 108 to about 117.

Clone DNA53978-1443 was deposited with ATCC on June 16, 1998, and is assigned ATCC deposit no. 209983.

Based on a BLAST and FastA sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO784 shows amino acid sequence identity to the following proteins: RNU42209_1,

MMU91538_1, CGU91742_1, CELF55A4_6, SC22_YEAST, and F48188.

EXAMPLE 33: Isolation of cDNA Clones Encoding Human PRO783

A yeast screening assay was employed to identify cDNA clones that encoded potential secreted proteins. Use of this yeast screening assay allowed identification of a single cDNA clone, designated herein as DNA45201 (Figure 80; SEQ ID NO:139).

The DNA45201 sequence was then used to search expressed sequence tag (EST) databases for the presence of potential homologies. The EST databases included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained is herein designated as "consen01". A proprietary Genentech EST sequence was used in the consensus assembly and is herein designated as DNA14575 (Figure 81; SEQ ID NO:140).

Based on the consen01 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO783. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GACTGTATCTGAGCCCCAGACTGC-3' (SEQ ID NO:141),

forward PCR primer 5'-TCAGCAATGAGGTGCTGCTC-3' (SEQ ID NO:142), and

reverse PCR primer 5'-TGAGGAAGATGAGGGACAGGTTGG-3' (SEQ ID NO:143).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consen01 sequence which had the following nucleotide sequence:

hybridization probe

5'-TATGGAAGCACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCC-3' (SEQ ID NO:144).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with a PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO783 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB228). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science,

253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO783 [herein designated as DNA53996-1442] (SEQ ID NO:137) and the derived protein sequence for PRO783.

The entire nucleotide sequence of DNA53996-1442 is shown in Figure 78 (SEQ ID NO:137). Clone
 5 DNA53996-1442 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 310-312 and ending at the stop codon at nucleotide positions 1777-1779 (Figure 78). The predicted polypeptide precursor is 489 amino acids long (Figure 79). The full-length PRO783 protein shown in Figure 79 has an estimated molecular weight of about 55,219 daltons and a pI of about 8.47. Analysis of the full-length PRO783 sequence shown in Figure 79 (SEQ ID NO:138) evidences the presence of the following features:
 10 transmembrane domains located at about amino acids 23-42, 67-89, 111-135, 154-176, 194-218, 296-319, 348-370, 387-410 and 427-452; leucine zipper patterns located at about amino acids 263-283 and 399-420; a potential tyrosine kinase phosphorylation site at about amino acids 180-187; potential N-glycosylation sites at about amino acids 105 -108 and 121-124; potential cAMP- and a cGMP-dependent protein kinase phosphorylation site at about amino acids 288-291; and a region having sequence identity with bacterial
 15 rhodopsins retinal binding site protein at about amino acids 190-218.

An analysis of the Dayhoff database (version 35.45 SwissProt 35) shows some sequence identity between the PRO783 amino acid sequence and the following Dayhoff sequences: YNC2_CAEEL, D64048, ATAC002332_3F4P9.3, NY2R_SHEEP, and VSH_MUMPA.

Clone DNA53996-1442 was deposited with the ATCC on June 2, 1998, and is assigned ATCC deposit
 20 no. 209921.

EXAMPLE 34: Isolation of cDNA Clones Encoding Human PRO820

An expressed sequence tag (EST) DNA database (Merck/Wash. U) was searched and an EST designated
 EST no. AA504080, Merck clone 825136, was identified (library 312, human B-cell tonsil). Homology searches
 25 revealed that this EST showed sequence identity with low affinity immunoglobulin gamma Fc receptor II. DNA sequencing gave the full-length DNA sequence for PRO820 and the derived protein sequence for PRO820.

The entire nucleotide sequence of DNA56041-1416 is shown in Figure 82 (SEQ ID NO:145). Clone
 DNA56041-1416 contains a single open reading frame with an apparent translational initiation site at nucleotide
 30 positions 115-117 and ending at the stop codon at nucleotide positions 487-489 (Figure 82). The predicted polypeptide precursor is 124 amino acids long (Figure 83). The full-length PRO820 protein shown in Figure 83 has an estimated molecular weight of about 14,080 daltons and a pI of about 7.48. Clone DNA56041-1416 has been deposited with ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Still analyzing the amino acid sequence of SEQ ID NO:146, the putative signal peptide is at about amino
 35 acids 1-15 of SEQ ID NO:146. Protein kinase C phosphorylation sites are at about amino acids 20-22 and 43-45 of SEQ ID NO:146. An N-myristoylation site is at about amino acids 89-94 of SEQ ID NO:146. An immunoglobulin and major histocompatibility complex domain is at about amino acids 83-90 of SEQ ID NO:146.

The corresponding nucleotides can be routinely determined given the sequences provided herein.

EXAMPLE 35: Isolation of cDNA Clones Encoding Human PRO1080

A consensus DNA sequence was assembled relative to other EST sequences using phrap and was extended using repeated cycles of BLAST and phrap so as to extend the consensus sequence as far as possible using the sources of the EST sequences as described in Example 1 above. The consensus sequence is designated herein as DNA52640. An EST proprietary to Genentech was employed in the consensus assembly and is herein designated as DNA36527 (Figure 86; SEQ ID NO:149).

In light of an observed sequence homology between the DNA36527 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 526423, the Merck EST clone 526423 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 84 and is herein designated as DNA56047-1456.

The entire nucleotide sequence of DNA56047-1456 is shown in Figure 84 (SEQ ID NO:147). Clone DNA56047-1456 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 159-161 and ending at the stop codon at nucleotide positions 1233-1235 of SEQ ID NO:147 (Figure 84). The predicted polypeptide precursor is 358 amino acids long (Figure 85). The full-length PRO1080 protein shown in Figure 85 has an estimated molecular weight of about 40,514 daltons and a pI of about 6.08. Clone DNA56047-1456 has been deposited with ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Also shown in Figure 85 are the approximate locations of the signal peptide, cell attachment site, Nt-DnaJ domain signature, region having sequence identity with Nt-DnaJ domain proteins, and N-glycosylation sites. The corresponding nucleic acids of these amino acid sequences and others provided herein can be routinely determined by the information provided herein.

EXAMPLE 36: Isolation of cDNA Clones Encoding Human PRO1079

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above, and is herein designated DNA52714. Based on information provided by the assembly, the clone for Merck EST no. HO6898 was obtained and sequenced, thereby giving the nucleotide sequence designated herein as DNA56050-1455. The entire nucleotide sequence of DNA56050-1455 is shown in Figure 87 (SEQ ID NO:150). Clone DNA56050-1455 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 183-185 and ending at the stop codon at nucleotide positions 861-863 (Figure 87). The predicted polypeptide precursor is 226 amino acids long (Figure 88). The full-length PRO1079 protein shown in Figure 88 has an estimated molecular weight of about 24,611 Daltons and a pI of about 4.85. Analysis of the full-length PRO1079 sequence shown in Figure 88 (SEQ ID NO:3) evidences the presence of the following features: a signal peptide at about amino acid 1-29; potential N-myristoylation sites at about amino acids 10-15, and 51-56; homology to photosystem I psaG and psaK proteins at about amino acids 2 to 20; and homology to prolyl endopeptidase family serine proteins at about amino acids 150 to 163.

Analysis of the amino acid sequence of the full-length PRO1079 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced some sequence identity between the PRO1079 amino acid sequence and the following Dayhoff sequences: CEK10C3_4, MMU50734_1, D69503, AF051149_1, and VSMP_CVMS.

Clone UNQ536 (DNA56050-1455) was deposited with the ATCC on June 22, 1998, and is assigned ATCC deposit no. 203011.

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EXAMPLE 37: Isolation of cDNA clones Encoding Human PRO793

A cDNA clone (DNA56110-1437) encoding a native human PRO793 polypeptide was identified by a yeast screen, in a human skin tumor cDNA library that preferentially represents the 5' ends of the primary cDNA clones. The yeast screen employed identified a single EST clone designated herein as DNA50177 (Figure 91; SEQ ID NO:154). The DNA50177 sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ[®], Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., *Methods in Enzymology*, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence is herein designated DNA50972.

In light of an observed sequence homology between the DNA50972 consensus sequence and an EST sequence encompassed within the Merck EST clone no. N33874, the Merck EST clone N33874 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 89 and is herein designated as DNA56110-1437.

The full-length DNA56110-1437 clone shown in Figure 89 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 77-79 and ending at the stop codon at nucleotide positions 491-493 (Figure 89). The predicted polypeptide precursor is 138 amino acids long (Figure 90). The full-length PRO793 protein shown in Figure 90 has an estimated molecular weight of about 15,426 daltons and a pI of about 10.67. Analysis of the full-length PRO793 sequence shown in Figure 90 (SEQ ID NO:153) evidences the presence of the following: transmembrane domains from about amino acid 12 to about amino acid 30, from about amino acid 33 to about amino acid 52, from about amino acid 69 to about amino acid 89 and from about amino acid 93 to about amino acid 109, potential N-myristoylation sites from about amino acid 11 to about amino acid 16, from about amino acid 51 to about amino acid 56 and from about amino acid 116 to about amino acid 121 and an amino acid sequence block having homology to an aminoacyl-transfer RNA synthetase class-II protein from about amino acid 49 to about amino acid 59. Clone DNA56110-1437 has been deposited with ATCC on August 11, 1998 and is assigned ATCC deposit no. 203113.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 90 (SEQ ID NO:153), evidenced certain homology between the PRO793 amino acid sequence and the following Dayhoff sequences: S47453, AF015193_12, MTEHGNS9_2, E64030, H69784, D64995, CD53_MOUSE, GEN8006, AE001138_7 and COX2_STRPU.

EXAMPLE 38: Isolation of cDNA Clones Encoding Human PRO1016

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. The consensus sequence obtained is herein designated DNA53502.

In light of an observed sequence homology between the DNA53502 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 38680, the Merck EST clone 38680 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 92.

The entire nucleotide sequence of DNA56113-1378 is shown in Figure 92 (SEQ ID NO:155). Clone DNA56113-1378 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 168-170 and ending at the stop codon at nucleotide positions 1302-1304 (Figure 92). The predicted polypeptide precursor is 378 amino acids long (Figure 93). The full-length PRO1016 protein shown in Figure 93 has an estimated molecular weight of about 44,021 daltons and a pI of about 9.07. Clone DNA56113-1378 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO1016 polypeptide suggests that portions of it possess sequence identity with acyltransferase, thereby indicating that PRO1016 may be a novel acyltransferase.

Still analyzing the amino acid sequence of SEQ ID NO:156, the putative signal peptide is at about amino acids 1-18 of SEQ ID NO:156. The transmembrane domain(s) are at about amino acids 332-352 and 305-330 of SEQ ID NO:156. The fructose-bisphosphate aldolase class-II protein homology sequence is at about amino acids 73-90 of SEQ ID NO:156. The extradiol ring-cleavage dioxygenase protein is at about amino acids 252-275 of SEQ ID NO:156. The corresponding nucleotides can be routinely determined given the sequences provided herein.

The specific Dayhoff database designation names of sequences to which PRO1016 has sequence identity with include the following: S52645, P_R59712, P_R99249, P_R59713, BNAGPATRF_1, CELT05H4_15 and CELZK40_1.

EXAMPLE 39: Isolation of cDNA Encoding Human PRO1013

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. The consensus DNA sequence was then extended using repeated cycles of BLAST and phrap to extend the consensus sequence as far as possible using the sources of EST sequences.

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3107695, the Incyte EST clone 3107695 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 94 and is herein designated as DNA56410-1414.

The entire nucleotide sequence of DNA56410-1414 is shown in Figure 94 (SEQ ID NO:157). Clone DNA56410-1414 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 17-19 and ending at the stop codon at nucleotide positions 1244-1246 (Figure 94). The predicted

polypeptide precursor is 409 amino acids long (Figure 95). The full-length PRO1013 protein shown in Figure 95 has an estimated molecular weight of about 46,662 daltons and a pI of about 7.18. Clone DNA56410-1414 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

5 Still analyzing the amino acid sequence of SEQ ID NO:158, the putative signal peptide is at about amino acids 1-19 of SEQ ID NO:158. N-glycosylation sites are at about amino acids 75-78 and 322-325 of SEQ ID NO:158. An N-myristoylation site is at about amino acids 184-189 of SEQ ID NO:158. A growth factor and cytokine receptor family domain is at about amino acids 134-149 of SEQ ID NO:158. The corresponding nucleotides can be routinely determined given the sequences provided herein.

10 Blast analysis showed some sequence identity with other proteins. Specifically, PRO1013 has some sequence identity with at least the Dayhoff sequences designated: D63877_1; MHU22019_1, AE000730_10, and AF019079_1.

EXAMPLE 40: Isolation of cDNA Clones Encoding Human PRO937

15 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. That consensus sequence is herein designated DNA49651. Based on the DNA49651 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO937.

PCR primers (forward and reverse) were synthesized:

20 forward PCR primer 5'-CTCCGTGGTAAACCCACAGCCC-3' (SEQ ID NO:161); and
reverse PCR primer 5'-TCACATCGATGGGATCCATGACCG-3' (SEQ ID NO:162).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA48651 sequence which had the following nucleotide sequence:

25 hybridization probe
 5'-GGTCTCGTGACTGTGAAGCCATGTTACAACACTACTGCTCAAACATCATGAG-3' (SEQ ID NO:163).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO937 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

30 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO937 [herein designated as DNA56436-1448] (SEQ ID NO:159) and the derived protein sequence for PRO937.

The entire nucleotide sequence of DNA56436-1448 is shown in Figure 96 (SEQ ID NO:159). It contains a single open reading frame having an apparent translational initiation site at nucleotide positions 499-501 and ending at the stop codon found at nucleotide positions 2167-2169 (Figure 96, SEQ ID NO:159). The predicted polypeptide precursor is 556 amino acids long, has a calculated molecular weight of approximately 62,412 daltons and an estimated pI of approximately 6.62. Analysis of the full-length PRO937 sequence shown

in Figure 97 (SEQ ID NO:160) evidences the presence of the following features: signal peptide at about amino acids 1-22; ATP/GTP-binding site motif A (P-loop) at about amino acids 515-523; a potential N-glycosylation site at about amino acids 514-517; and sites of glypican homology at about amino acids 54-74, 106-156, 238-279, 309-345, 423-459, and 468-505.

5 Clone DNA56436-1448 has been deposited with ATCC on May 27, 1998, and is assigned ATCC deposit no. 209902.

Analysis of the amino acid sequence of the full-length PRO937 polypeptide suggests that it possesses significant sequence similarity to glypican proteins, thereby indicating that PRO937 may be a novel glypican protein. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO937 amino acid sequence and the following Dayhoff sequences:

10 GPCCK_MOUSE, GPC2_RAT, GPC5_HUMAN, GPC3_HUMAN, P_R30168, CEC03H12_2, GEN13820, HS119E23_1, HDAC_DROME, and AF017637_1.

EXAMPLE 41: Isolation of cDNA clones Encoding Human PRO842

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single

15 Incyte EST cluster sequence designated herein as Incyte EST cluster sequence no. 69572. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a

20 BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA54230.

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA477092, the Merck EST clone AA477092 was purchased and

25 the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 98 and is herein designated as DNA56855-1447.

The full length clone shown in Figure 98 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 153-155 and ending at the stop codon found at nucleotide positions 510-512 (Figure 98; SEQ ID NO:164). The predicted polypeptide precursor (Figure 99, SEQ ID

30 NO:165) is 119 amino acids long. PRO842 has a calculated molecular weight of approximately 13,819 Daltons and an estimated pI of approximately 11.16. Other features of PRO842 include a signal peptide at about amino acids 1-22, a potential protein kinase C phosphorylation site at about amino acids 39-41 and two potential N-myristoylation sites at about amino acids 27-32 and about amino acids 46-51.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence

35 alignment analysis of the full-length sequence shown in Figure 98 (SEQ ID NO:164), evidenced some homology between the PRO842 amino acid sequence and the following Dayhoff sequences: CEZK131_1, P_R80843, RAT5HT2X_1, S81882_1, A60912, MCU60315_137MC137L, U93422_1, p_P91996, U93462_1, and

ZN18_HUMAN.

Clone DNA56855-1447 was deposited with the ATCC on June 23, 1998, and is assigned ATCC deposit no. 203004.

EXAMPLE 42: Isolation of cDNA clones Encoding Human PRO839

5 Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte LIFESEQ® database, designated Incyte EST Cluster No. 24479. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using
10 the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55709.

15 In light of an observed sequence homology between the DNA55709 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 754525, the Merck EST clone 754525 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 100 and is herein designated as DNA56859-1445.

20 The full length clone shown in Figure 100 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 2-4 and ending at the stop codon found at nucleotide positions 263-265 (Figure 100; SEQ ID NO:166). The predicted polypeptide precursor (Figure 101, SEQ ID NO:167) is 87 amino acids long. PRO839 has a calculated molecular weight of approximately 9,719 Daltons and an estimated pI of approximately 4.67. Other features of PRO839 include a signal peptide at about amino acids 1-23, potential protein kinase C phosphorylation sites at about amino acids 37-39 and about amino acids 85-87,
25 a potential casein kinase II phosphorylation site at about amino acids 37-40, sequence identity with ribonucleotide reductase large subunit protein at about amino acids 50-60, and sequence identity with eukaryotic RNA-binding region RNP-1 proteins at about amino acids 70-79.

30 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 101 (SEQ ID NO:167), evidenced some homology between the PRO839 amino acid sequence and the following Dayhoff sequences: CD14_MOUSE, XPR6_YARLI, HS714385_1, S49783, BB19_RABIT, GVPH-HALME, AB003135_1, P_R85453, LUU27081_2, and TP2B_MOUSE.

Clone DNA56859-1445 was deposited with the ATCC on June 23, 1998, and is assigned ATCC deposit no.209019.

35

EXAMPLE 43: Isolation of cDNA Clones Encoding Human PRO1180

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence (Incyte EST cluster sequence no. 14732). The Incyte EST cluster sequence no. 14732 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55711.

In light of an observed sequence homology between the DNA55711 consensus sequence and an EST sequence encompassed within the Merck EST clone no. T60981, the Merck EST clone T60981 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 102 and is herein designated DNA56860-1510.

The full length clone shown in Figure 102 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 78-80 and ending at the stop codon found at nucleotide positions 909-911 (Figure 102; SEQ ID NO:168). The predicted polypeptide precursor is 277 amino acids long, has a calculated molecular weight of approximately 31,416 daltons and an estimated pI of approximately 8.88. Analysis of the full-length PRO1180 sequence shown in Figure 103 (SEQ ID NO:169) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 23, a leucine zipper pattern sequence from about amino acid 10 to about amino acid 31, and potential N-myristoylation sited from about amino acid 64 to about amino acid 69, from about amino acid 78 to about amino acid 83, from about amino acid 80 to about amino acid 85, from about amino acid 91 to about amino acid 96 and from about amino acid 201 to about amino acid 206. Clone DNA56860-1510 has been deposited with the ATCC on June 9, 1998 and is assigned ATCC deposit no. 209952.

Analysis of the amino acid sequence of the full-length PRO1180 polypeptide suggests that it possesses sequence similarity to the methyltransferase family of proteins. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO1180 amino acid sequence and the following Dayhoff sequences, MTC165_14, D69267, YH09_YEAST, BIOC_SERMA, ATAC00448415T1D16.16, SHGCPIR_18, SPBC3B9_4, AB009504_14, P_W17977 and A69952.

EXAMPLE 44: Isolation of cDNA clones Encoding Human PRO1134

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 7511. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or

in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55725. Two proprietary Genentech EST sequences were employed in the assembly and are shown in Figure 106 (SEQ ID NO:172) and Figure 107 (SEQ ID NO:173).

5 In light of an observed sequence homology between the DNA55725 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H94897, the Merck EST clone H94897 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 106 and is herein designated as DNA56865-1491.

10 Clone DNA56865-1491 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 153-155 and ending at the stop codon at nucleotide positions 1266-1268 (Figure 104). The predicted polypeptide precursor is 371 amino acids long (Figure 105). The full-length PRO1134 protein shown in Figure 105 has an estimated molecular weight of about 41,935 daltons and a pI of about 9.58. Analysis of the full-length PRO1134 sequence shown in Figure 105 (SEQ ID NO:171) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 23, potential N-glycosylation sites from
15 about amino acid 103 to about amino acid 106, from about amino acid 249 to about amino acid 252 and from about amino acid 257 to about amino acid 260, and an amino acid block having homology to tyrosinase CuA-binding region proteins from about amino acid 280 to about amino acid 306. Clone DNA56865-1491 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203022.

20 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 105 (SEQ ID NO:171), evidenced significant homology between the PRO1134 amino acid sequence and the following Dayhoff sequences: F20P5_18, AC002396_10, S47847, C64146, GSPA_BACSU, P_W10564, RFAI_ECOLI, Y258_HAEIN, RFAJ_SALTY and P_R32985.

25 EXAMPLE 45: Isolation of cDNA clones Encoding Human PRO830

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incytedatabase, designated 20251. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing
30 homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55733.

35 In light of an observed sequence homology between the DNA55733 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H78534, the Merck EST clone H78534 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.

The sequence of this cDNA insert is shown in Figure 108 and is herein designated as DNA56866-1342.

Clone DNA56866-1342 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 154-156 and ending at the stop codon at nucleotide positions 415-417 (Figure 108). The predicted polypeptide precursor is 87 amino acids long (Figure 109). The full-length PRO830 protein shown in Figure 109 has an estimated molecular weight of about 9,272 daltons and a pI of about 9.19. Analysis of the full-length PRO830 sequence shown in Figure 109 (SEQ ID NO:175) evidences the presence of the following:

5 a signal peptide from about amino acid 1 to about amino acid 33, potential N-myristoylation sites from about amino acid 2 to about amino acid 7 and from about amino acid 8 to about amino acid 13 and a thioredoxin family of proteins homology block from about amino acid 23 to about amino acid 39. Clone UNQ470 (DNA56866-1342) has been deposited with ATCC on June 22, 1998 and is assigned ATCC deposit no. 203023.

10 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 109 (SEQ ID NO:175), evidenced significant homology between the PRO830 amino acid sequence and the following Dayhoff sequences: HSU88154_1, HSU88153_1, SAPKSGENE_1, HPU31791_5, GGCNOT2_1, CPU91421_1, CHKESTPC09_1, PQ0769, U97553_79 and B60095.

15

EXAMPLE 46: Isolation of cDNA clones Encoding Human PRO1115

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated Incyte EST cluster sequence no. 165008. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55726.

25 In light of an observed sequence homology between the DNA55726 consensus sequence and an EST sequence encompassed within the Merck EST clone no. R75784, the Merck EST clone R75784 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.

30 The sequence of this cDNA insert is shown in Figure 111 and is herein designated as DNA56868-1478.

The full length clone shown in Figure 110 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 189-191 and ending at the stop codon found at nucleotide positions 1524-1526 (Figure 110; SEQ ID NO:176). The predicted polypeptide precursor (Figure 111, SEQ ID NO:177) is 445 amino acids long. PRO1115 has a calculated molecular weight of approximately 50,533 Daltons and an estimated pI of approximately 8.26. Additional features include a signal peptide at about amino acids 1-20; potential N-glycosylation sites at about amino acids 204-207, 295-298, and 313-316; and putative transmembrane domains at about amino acids 35-54, 75-97, 126-146, 185-204, 333-350, and 353-371.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 111 (SEQ ID NO:177), evidenced some amino acid sequence identity between the PRO1115 amino acid sequence and the following Dayhoff sequences: AF053947_79, S73698, CEC47A10_4, CCOMTNDSSG_1, HS4LMP2AC_1, LMP2_EBV, PA24_MOUSE, HCU33331_7, P-W05508, and AF002273_1.

- 5 Clone DNA56868-1478 was deposited with the ATCC on June 23, 1998 and is assigned ATCC deposit no. 203024..

EXAMPLE 47: Isolation of cDNA clones Encoding Human PRO1277

- 10 A consensus DNA sequence was assembled relative to other ESTs using repeated cycles of BLAST and the program "phrap" as described in Example 1 above. One or more of the ESTs from the assembly was derived from diseased coronary artery tissue. The consensus sequence obtained is designated herein as "DNA49434".

- 15 In light of an observed sequence homology between the DNA49434 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3042605, the Incyte EST clone 3042605 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 112 (SEQ ID NO:178).

- 20 Clone DNA56869-1545 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 188-190, and an apparent stop codon at nucleotide positions 2222-2224 (Figure 112). The predicted polypeptide precursor is 678 amino acids long (Figure 113). The full-length PRO1277 protein shown in Figure 113 has an estimated molecular weight of about 73,930 daltons and a pI of about 9.48. Additional features include a signal peptide at about amino acids 1-26; a transmembrane domain at about amino acids 181-200, and potential N-glycosylation sites at about amino acids 390-393 and 520-523.

- 25 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 113 (SEQ ID NO:179), revealed significant homology between the PRO1277 amino acid sequence and Dayhoff sequence no AF012252_1. Homology was also found between the PRO1277 amino acid sequence and the following Dayhoff sequences: AF006740_1, CA36_HUMAN, HSU1_1, HUMCOL7A1X_1, CA17_HUMAN, MMZ78163_1, CAMA_CHICK, HSU69263_1, YNX3_CAEEL, and MMRNAM3_1.

- 30 Clone DNA56869-1545 has been deposited with ATCC and is assigned ATCC deposit no. 203161.

EXAMPLE 48: Isolation of cDNA Clones Encoding Human PRO1135

- 35 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA52767. Based on the DNA52767 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1135.

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with PCR primer pairs prepared based upon the DNA52767 sequence. A positive library was then used to isolate clones encoding the PRO1135 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human coronary artery smooth muscle tissue (LIB309). The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1135 [herein designated as DNA56870-1492] (SEQ ID NO:180) and the derived protein sequence for PRO1135.

The entire nucleotide sequence of DNA56870-1492 is shown in Figure 114 (SEQ ID NO:180). Clone DNA56870-1492 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 62-64 and ending at the stop codon at nucleotide positions 1685-1687 (Figure 114). The predicted polypeptide precursor is 541 amino acids long (Figure 115). The full-length PRO1135 protein shown in Figure 115 has an estimated molecular weight of about 60,335 daltons and a pI of about 5.26. Analysis of the full-length PRO1135 sequence shown in Figure 115 (SEQ ID NO:181) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 21, potential N-glycosylation sites from about amino acid 53 to about amino acid 56, from about amino acid 75 to about amino acid 78, from about amino acid 252 to about amino acid 255 and from about amino acid 413 to about amino acid 416 and an amino acid block having homology to glycosyl hydrolase family 35 proteins from about amino acid 399 to about amino acid 414. Clone DNA56870-1492 has been deposited with ATCC on June 2, 1998 and is assigned ATCC deposit no. 209925.

Analysis of the amino acid sequence of the full-length PRO1135 polypeptide suggests that it possesses significant sequence similarity to the alpha 1,2-mannosidase protein, thereby indicating that PRO1135 may be a novel mannosidase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO1135 amino acid sequence and the following Dayhoff sequences, DMC86E4_5, D86967_1, SPAC23A1_4, YH04_YEAST, B54408, SSMAN9MAN_1, CEZC410_4, S61631 and MSU14190_1.

EXAMPLE 49: Isolation of cDNA Clones Encoding Human PRO1114

A cDNA sequence isolated in the amylase screen described in Example 2 above was found, by the WU-BLAST-2 sequence alignment computer program, to have certain sequence identity to other known interferon receptors. This cDNA sequence is herein designated DNA48466 and is shown in Figure 118 (SEQ ID NO:184).

Based on the sequence identity, probes were generated from the sequence of the DNA48466 molecule and used to screen a human breast carcinoma library (LIB135) prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes

et al., *Science*, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

The oligonucleotide probes employed were as follows:

forward PCR primer 5'-AGGCTTCGCTGCGACTAGACCTC-3' (SEQ ID NO:185)

reverse PCR primer 5'-CCAGGTCGGGTAAGGATGGTTGAG-3' (SEQ ID NO:186)

hybridization probe

- 5 5'-TTTCTACGCATTGATTCCATGTTTGCTCACAGATGAAGTGGCCATTCTGC-3' (SEQ ID NO:187)

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 250-252, and a stop signal at nucleotide positions 1183-1185 (Figure 116, SEQ ID NO:182). The predicted polypeptide precursor is 311 amino acids long, has a calculated molecular weight of approximately 35,076 daltons and an estimated pI of approximately 5.04. Analysis of the full-length PRO1114 interferon receptor sequence shown in Figure 117 (SEQ ID NO:183) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 29, a transmembrane domain from about amino acid 230 to about amino acid 255, potential N-glycosylation sites from about amino acid 40 to about amino acid 43 and from about amino acid 134 to about amino acid 137, an amino acid sequence block having homology to tissue factor proteins from about amino acid 92 to about amino acid 119 and an amino acid sequence block having homology to integrin alpha chain proteins from about amino acid 232 to about amino acid 262. Clone DNA57033-1403 has been deposited with ATCC on May 27, 1998 and is assigned ATCC deposit no. 209905.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 117 (SEQ ID NO:183), evidenced significant homology between the PRO1114 interferon receptor amino acid sequence and the following Dayhoff sequences: G01418, INR1_MOUSE, P_R71035, INGS_HUMAN, A26595_1, A26593_1, I56215 and TF_HUMAN.

EXAMPLE 50: Isolation of cDNA Clones Encoding Human PRO828

A consensus DNA sequence was identified using the method described in Example 1 above. This consensus sequence is herein designated DNA35717. Based on the DNA35717 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO828.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GCAGGACTTCTACGACTTCAAGGC-3' (SEQ ID NO:190); and

- 30 reverse PCR primer 5'-AGTCTGGGCCAGGTACTTGAAGGC-3' (SEQ ID NO:191).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35717 sequence which had the following nucleotide sequence:

hybridization probe

5'-CAACATCCGGGGCAAACCTGGTGTGCTGGAGAAGTACCGCGGATCGGTGT-3' (SEQ ID NO:192)

35 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO828 gene using the probe oligonucleotide and one of the PCR primers. RNA

for construction of the cDNA libraries was isolated from human fetal lung tissue (LIB25).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO828 [herein designated as DNA57037-1444] (SEQ ID NO:188) and the derived protein sequence for PRO828.

The entire nucleotide sequence of DNA57037-1444 is shown in Figure 119 (SEQ ID NO:188). Clone
5 DNA57037-1444 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 34-36 and ending at the stop codon at nucleotide positions 595-597 (Figure 119). The predicted polypeptide precursor is 187 amino acids long (Figure 120). The full-length PRO828 protein shown in Figure 120 has an estimated molecular weight of about 20,996 daltons and a pI of about 8.62. Analysis of the full-length PRO828 sequence shown in Figure 120 (SEQ ID NO:189) evidences the presence of the following: a
10 signal peptide at about amino acids 1- 21; sequences identity to glutathione peroxidases signature 2 at about amino acids 82-89; sequence identity to glutathione peroxidases selenocysteine proteins at about amino acids 35-60, 63-100, 107-134, and 138-159. Clone DNA57037-1444 has been deposited with ATCC on May 27, 1998, and is assigned ATCC deposit no. 209903.

Analysis of the amino acid sequence of the full-length PRO828 polypeptide suggests that it possesses
15 significant sequence similarity to glutathione peroxidases, thereby indicating that PRO828 may be a novel peroxidase enzyme. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO828 amino acid sequence and the following Dayhoff sequences: AF053311_1, CELT09A12_2, AC004151_3, BTUE_ECOLI, CER05H10_3, P_P80918, PWU88907_1, and P_W22308.

20

EXAMPLE 51: Isolation of cDNA clones Encoding Human PRO1009

A cDNA clone (DNA57129-1413) encoding a native human PRO1009 polypeptide was identified by the use of a yeast screen, in a human SK-Lu-1 adenocarcinoma cell line cDNA library that preferentially represents the 5' ends of the primary cDNA clones. First SEQ ID NO:195 (Figure 123) was identified, which
25 was extended by alignments to other EST sequences to form a consensus sequence. Oligonucleotide probes based upon the consensus sequence were synthesized and used to screen the cDNA library which gave rise to the full-length DNA57129-1413 clone.

The full length DNA57129-1413 clone shown in Figure 121 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 41-43 and ending at the stop codon found at
30 nucleotide positions 1886-1888 (Figure 121; SEQ ID NO:193). The predicted polypeptide precursor (Figure 122, SEQ ID NO:194) is 615 amino acids long. Figure 122 also shows the approximate locations of the signal sequence, transmembrane domains, myristoylation sites, a glycosylation site and an AMP-binding domain. PRO1009 has a calculated molecular weight of approximately 68,125 daltons and an estimated pI of approximately 7.82. Clone DNA57129-1413 has been deposited with ATCC and is assigned ATCC deposit no.
35 209977. It is understood that the deposited clone has the actual and correct sequence and that the representations herein may have minor, normal sequencing errors.

Based on a WU-BLAST-2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1009 shows amino acid sequence identity to at least the following proteins which were designated in a Dayhoff database as follows: F69893, CEF28F8_2, BSY13917_7, BSY13917_7, D69187, D69649, XCRPFB_1, E64928, YDID_ECOLI, BNACSF8_1 and RPU75363_2.

5 EXAMPLE 52: Isolation of cDNA Clones Encoding Human PRO1007

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated as DNA40671.

In light of an observed sequence homology between the DNA40671 consensus sequence and an EST sequence encompassed within the Merck EST clone no. T70513, the Merck EST clone T70513 was purchased
10 and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 124.

The entire nucleotide sequence of DNA57690-1374 is shown in Figure 124 (SEQ ID NO:196). Clone DNA57690-1374 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 16-18 and ending at the stop codon at nucleotide positions 1054-1056 (Figure 124). The predicted
15 polypeptide precursor is 346 amino acids long (Figure 125). The full-length PRO1007 protein shown in Figure 125 has an estimated molecular weight of about 35,971 daltons and a pI of about 8.17. Clone DNA57690-1374 has been deposited with the ATCC on June 9, 1998. Regarding the sequence, it is understood that the deposited clone contains the actual sequence, and the sequences provided herein are based on known sequencing techniques. The representative figures herein show the representative numbering.

20 Analysis of the amino acid sequence of the full-length PRO1007 polypeptide suggests that portions of it possess sequence identity to MAGPIAP, thereby indicating that PRO1007 may be a novel member of the family to which MAGPIAP belongs.

Still analyzing the amino acid sequence of SEQ ID NO:197, the putative signal peptide is at about amino acids 1-30 of SEQ ID NO:197. The transmembrane domain is at amino acids 325-346 of SEQ ID NO:197. N-
25 glycosylation sites are at about amino acids 118-121, 129-132, 163-166, 176-179, 183-186 and 227-130 of SEQ ID NO:197. Ly-6/u-Par domain protein homology is at about amino acids 17-36 and 209-222 of SEQ ID NO:197. The corresponding nucleotides of the amino acids presented herein can be routinely determined given the sequences provided herein.

30 EXAMPLE 53: Isolation of cDNA clones Encoding Human PRO1056

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated herein as 6425. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify
35 existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a

consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55736.

In light of an observed sequence homology between the DNA55736 consensus sequence and an EST sequence encompassed within the Merck EST clone no. R88049, the Merck EST clone R88049 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.

- 5 The sequence of this cDNA insert is shown in Figure 126 and is herein designated as DNA57693-1424.

Clone DNA57693-1424 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 56-58 and ending at the stop codon at nucleotide positions 416-418 (Figure 126). The predicted polypeptide precursor is 120 amino acids long (Figure 127). The full-length PRO1056 protein shown in Figure 127 has an estimated molecular weight of about 13,345 daltons and a pI of about 5.18. Analysis of the full-length PRO1056 sequence shown in Figure 127 (SEQ ID NO:199) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 18, a transmembrane domain from about amino acid 39 to about amino acid 58, a potential N-glycosylation site from about amino acid 86 to about amino acid 89, protein kinase C phosphorylation sites from about amino acid 36 to about amino acid 38 and from about amino acid 58 to about amino acid 60, a tyrosine kinase phosphorylation site from about amino acid 25 to about amino acid 32 and an amino acid sequence block having homology to channel forming colicin proteins from about amino acid 24 to about amino acid 56. Clone DNA57693-1424 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203008.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 127 (SEQ ID NO:199), evidenced significant homology between the PRO1056 amino acid sequence and the following Dayhoff sequences: PLM_HUMAN, A40533, ATNG_HUMAN, A55571, ATNG_SHEEP, S31524, GEN13025, RIC_MOUSE, A48678 and A10871_1.

EXAMPLE 54: Isolation of cDNA clones Encoding Human PRO826

25 Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 47283. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56000.

35 In light of an observed sequence homology between the DNA56000 consensus sequence and an EST sequence encompassed within the Merck EST clone no. W69233, the Merck EST clone W69233 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 128 and is herein designated as DNA57694-1341.

Clone DNA57694-1341 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 13-15 and ending at the stop codon at nucleotide positions 310-312 (Figure 128). The predicted polypeptide precursor is 99 amino acids long (Figure 129). The full-length PRO826 protein shown in Figure 129 has an estimated molecular weight of about 11,050 daltons and a pI of about 7.47. Analysis of the full-length PRO826 sequence shown in Figure 129 (SEQ ID NO:201) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 22, potential N-myristoylation sites from about amino acid 22 to about amino acid 27 and from about amino acid 90 to about amino acid 95 and an amino acid sequence block having homology to peroxidase from about amino acid 16 to about amino acid 48. Clone DNA57694-1341 has been deposited with ATCC on June 22, 1998 and is assigned ATCC deposit no. 203017.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 129 (SEQ ID NO:201), evidenced significant homology between the PRO826 amino acid sequence and the following Dayhoff sequences: CCU12315_1, SCU96108_6, CELF39F10_4 and HELT_HELHO.

EXAMPLE 55: Isolation of cDNA clones Encoding Human PRO819

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 49605. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56015.

In light of an observed sequence homology between the DNA56015 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H65785, the Merck EST clone H65785 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 130 and is herein designated as DNA57695-1340.

Clone DNA57695-1340 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 46-48 and ending at the stop codon at nucleotide positions 202-204 (Figure 130). The predicted polypeptide precursor is 52 amino acids long (Figure 131). The full-length PRO819 protein shown in Figure 131 has an estimated molecular weight of about 5,216 daltons and a pI of about 4.67. Analysis of the full-length PRO819 sequence shown in Figure 131 (SEQ ID NO:203) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 24, a potential N-myristoylation site from about amino acid 2 to about amino acid 7 and a region having homology to immunoglobulin light chain from about amino acid 5 to about amino acid 33. Clone DNA57695-1340 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203006.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 131 (SEQ ID NO:203), evidenced significant homology between the PRO819 amino acid sequence and the following Dayhoff sequences: HSU03899_1, HUMIGLITEB_1, VG28_HSVSA, AF031522_1, PAD1_YEAST and AF045484_1.

5 EXAMPLE 56: Isolation of cDNA Clones Encoding Human PRO1006

An initial candidate sequence from Incyte cluster sequence no. 45748 was identified using the signal algorithm process described in Example 3 above. This sequence was then aligned with a variety of public and Incyte EST sequences and a consensus sequence designated herein as DNA56036 was derived therefrom.

10 In light of an observed sequence homology between the DNA56036 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 489737, the Merck EST clone 489737 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 132.

The entire nucleotide sequence of DNA57699-1412 is shown in Figure 132 (SEQ ID NO:204). Clone DNA57699-1412 contains a single open reading frame with an apparent translational initiation site at nucleotide
15 positions 28-30 and ending at the stop codon at nucleotide positions 1204-1206 (Figure 132). The predicted polypeptide precursor is 392 amino acids long (Figure 133). The full-length PRO1006 protein shown in Figure 133 has an estimated molecular weight of about 46,189 daltons and a pI of about 9.04. Clone DNA57699-1412 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

20 Analyzing the amino acid sequence of SEQ ID NO:205, the putative signal peptide is at about amino acids 1-23 of SEQ ID NO:205. The N-glycosylation sites are at about amino acids 40-43, 53-56, 204-207 and 373-376 of SEQ ID NO:205. An N-myristoylation site is at about amino acids 273-278 of SEQ ID NO:205.

The corresponding nucleotides of these amino acid regions and others can be routinely determined given the sequences provided herein.

25

EXAMPLE 57: Isolation of cDNA Clones Encoding Human PRO1112

Use of the signal sequence algorithm described in Example 3 above allowed identification of a specific EST cluster sequence. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database
30 (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is
35 herein designated DNA56018.

In light of an observed sequence homology between the DNA56018 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA223546, the Merck EST clone AA223546 was

purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 134 and is herein designated as DNA57702-1476.

The entire nucleotide sequence of DNA57702-1476 is shown in Figure 134 (SEQ ID NO:206). Clone DNA57702-1476 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 20-22 and ending at the stop codon at nucleotide positions 806-808 of SEQ ID NO:206 (Figure 134).

- 5 The predicted polypeptide precursor is 262 amino acids long (Figure 135). The full-length PRO1112 protein shown in Figure 135 has an estimated molecular weight of about 29,379 daltons and a pI of about 8.93. Figure 135 also shows the approximate locations of the signal peptide and transmembrane domains. Clone DNA57702-1476 has been deposited with the ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

- 10 Analysis of the amino acid sequence of the full-length PRO1112 polypeptide suggests that it possesses some sequence similarity to other proteins. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some sequence identity between the PRO1112 amino acid sequence and at least the following Dayhoff sequences, MTY20B11_13 (a mycobacterium tuberculosis peptide), F64471, AE000690_6, XLU16364_1, E43259 (H⁺-transporting ATP synthase) and PIGSLADRXE_1 (MHC class II histocompatibility antigen).

EXAMPLE 58: Isolation of cDNA clones Encoding Human PRO1074

- Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence (Incyte cluster sequence No. 42586). This cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQTM, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56251.

- 25 In light of an observed sequence homology between the DNA56251 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA081912, the Merck EST clone AA081912 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 136 and is the full-length DNA sequence for PRO1074. Clone DNA57704-1452 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209953.

- 30 The entire nucleotide sequence of DNA57704-1452 is shown in Figure 136 (SEQ ID NO:208). Clone DNA57704-1452 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 322-324 and ending at the stop codon at nucleotide positions 1315-1317 (Figure 136). The predicted polypeptide precursor is 331 amino acids long (Figure 137). The full-length PRO1074 protein shown in Figure 137 has an estimated molecular weight of about 39,512 Daltons and a pI of about 8.03. Analysis of the full-

length PRO1074 sequence shown in Figure 137 (SEQ ID NO:209) evidences the presence of the following features: a transmembrane domain at about amino acids 20 to 39; potential N-glycosylation sites at about amino acids 72 to 75, 154 to 157, 198 to 201, 212 to 215, and 326 to 329; a glycosaminoglycan attachment site at about amino acids 239 to 242, and a Ly-6/u-PAR domain at about amino acids 23 to 36.

Analysis of the amino acid sequence of the full-length PRO1074 polypeptide suggests that it possesses significant sequence similarity to beta 1,3-galactosyltransferase, thereby indicating that PRO1074 may be a novel member of the galactosyltransferase family of proteins. Analysis of the amino acid sequence of the full-length PRO1074 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1074 amino acid sequence and the following Dayhoff sequences: AF029792_1, P_R57433, DMU41449_1, AC000348_14, P_R47479, CET09F5_2, CEF14B6_4, CET15D6_5, CEC54C8_4, and CEE03H4_10.

Clone DNA57704-1452 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209953.

EXAMPLE 59: Isolation of cDNA clones Encoding Human PRO1005

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, Incyte cluster sequence no. 49243. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56380.

In light of an observed sequence homology between the DNA56380 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA256657, the Merck EST clone AA256657 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 138 and is herein designated as DNA57708-1411.

The full length clone shown in Figure 138 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 30-32 and ending at the stop codon found at nucleotide positions 585-587 (Figure 138; SEQ ID NO:210). The predicted polypeptide precursor (Figure 139, SEQ ID NO:211) is 185 amino acids long. PRO1005 has a calculated molecular weight of approximately 20,331 daltons and an estimated pI of approximately 5.85. Clone DNA57708-1411 was deposited with the ATCC June 23, 1998, and is assigned ATCC deposit no. 203021.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 139 (SEQ ID NO:211), evidenced some homology between the PRO1005 amino acid sequence and the following Dayhoff sequences: DDU07187_1, DDU87912_1, CELD1007_14, A42239, DDU42597_1, CYAG_DICDI, S50452, MRKC_KLEPN, P-R41998,

and XYNA_RUMFL.

EXAMPLE 60: Isolation of cDNA clones Encoding Human PRO1073

An initial DNA sequence referred to herein as DNA55938 and shown in Figure 142 (SEQ ID NO:214) was identified using a yeast screen, in a human SK-Lu-1 adenocarcinoma cell line cDNA library that preferentially represents the 5' ends of the primary cDNA clones. DNA55938 was then compared to ESTs from public databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA), using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. The ESTs were clustered and assembled into a consensus DNA sequence using the computer program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained is designated herein as DNA56411.

In light of an observed sequence homology between the DNA56411 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H86027, the Merck EST clone H86027 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 140.

The full length DNA57710-1451 clone shown in Figure 140 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 345-347 and ending at the stop codon found at nucleotide positions 1242-1244 (Figure 140; SEQ ID NO:212). The predicted polypeptide precursor (Figure 141, SEQ ID NO:213) is 299 amino acids long. PRO1073 has a calculated molecular weight of approximately 34,689 daltons and an estimated pI of approximately 11.49. The PRO1073 polypeptide has the following additional features: a signal peptide at about amino acids 1-31, sequence identity to bZIP transcription factor basic domain signature at about amino acids, a potential N-glycosylation site at about amino acids 2-5, and sequence identity with protamine P1 proteins at about amino acids 158-183.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 141 (SEQ ID NO:213), revealed some sequence identity between the PRO1073 amino acid sequence and the following Dayhoff sequences: MMU37351_1, ATAC00250510T9J22.10, S59043, ENXNUPR_1, B47328, SR55_DROME, S26650, SON_HUMAN, VIT2_CHICK, and XLC4SRPRT_1.

Clone DNA57710-1451 was deposited with the ATCC on July 1, 1998 and is assigned ATCC deposit no. 203048.

EXAMPLE 61: Isolation of cDNA clones Encoding Human PRO1152

A cDNA clone (DNA57711-1501) encoding a native human PRO1152 polypeptide was identified by employing a yeast screen, in a human infant brain cDNA library that preferentially represents the 5' ends of the primary cDNA clones. Specifically, a yeast screen was employed to identify a cDNA designated herein as DNA55807 (SEQ ID NO:217; see Figure 145).

In light of an observed sequence homology between the DNA55807 sequence and an EST sequence encompassed within the Merck EST clone no. R56756, the Merck EST clone R56756 was purchased and the

cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 143.

The full-length DNA57711-1501 clone shown in Figure 143 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 58-60 and ending at the stop codon at nucleotide positions 1495-1497 (Figure 143). The predicted polypeptide precursor is 479 amino acids long (Figure 144).

- 5 The full-length PRO1152 protein shown in Figure 144 has an estimated molecular weight of about 53,602 daltons and a pI of about 8.82. Analysis of the full-length PRO1152 sequence shown in Figure 144 (SEQ ID NO:216) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, transmembrane domains from about amino acid 133 to about amino acid 155, from about amino acid 168 to about amino acid 187, from about amino acid 229 to about amino acid 247, from about amino acid 264 to about amino acid 285, from about amino acid 309 to about amino acid 330, from about amino acid 371 to about amino acid 390 and from about amino acid 441 to about amino acid 464, potential N-glycosylation sites from about amino acid 34 to about amino acid 37 and from about amino acid 387 to about amino acid 390 and an amino acid sequence block having homology to a respiratory-chain NADH dehydrogenase subunit from about amino acid 243 to about amino acid 287. Clone DNA57711-1501 has been deposited with ATCC on July 1, 1998 and is assigned ATCC deposit no. 203047.

- 15 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST-2 sequence alignment analysis of the full-length sequence shown in Figure 144 (SEQ ID NO:216), evidenced significant homology between the PRO1152 amino acid sequence and the following Dayhoff sequences: AF052239_1, SYNN9CGA_1, SFCYTB2_1, GEN12507, P_R11769, MTV025_109, C61168, S43171, P_P61689 and P_P61696.

EXAMPLE 62: Isolation of cDNA clones Encoding Human PRO1136

- Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 109142. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56039.

- In light of an observed sequence homology between the DNA56039 consensus sequence and an EST sequence encompassed within the Merck EST clone no. HSC1NF011, the Merck EST clone HSC1NF011 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 146 and is herein designated as DNA57827-1493.

Clone DNA57827-1493 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 216-218 and ending at the stop codon at nucleotide positions 2112-2114 (Figure 146).

The predicted polypeptide precursor is 632 amino acids long (Figure 147). The full-length PRO1136 protein shown in Figure 147 has an estimated molecular weight of about 69,643 daltons and a pI of about 8.5. Analysis of the full-length PRO1136 sequence shown in Figure 147 (SEQ ID NO:219) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15 and potential N-glycosylation sites from about amino acid 108 to about amino acid 111, from about amino acid 157 to about amino acid 160, from about amino acid 289 to about amino acid 292 and from about amino acid 384 to about amino acid 387. Clone DNA57827-1493 has been deposited with ATCC on July 1, 1998 and is assigned ATCC deposit no. 203045.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 147 (SEQ ID NO:219), evidenced significant homology between the PRO1136 amino acid sequence and the following Dayhoff sequences: AF034746_1, AF034745_1, MMAF000168_19, HSMUPP1_1, AF060539_1, SP97_RAT, I38757, MMU93309_1, CEK01A6_4 and HSA224747_1.

EXAMPLE 63: Isolation of cDNA clones Encoding Human PRO813

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence (Incyte EST cluster sequence no. 45501. The Incyte EST cluster sequence no. 45501 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56400.

In light of an observed sequence homology between the DNA56400 consensus sequence and an EST sequence encompassed within the Merck EST clone no. T90592, the Merck EST clone T90592 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 148 and is herein designated DNA57834-1339.

The full length clone shown in Figure 148 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 109-111 and ending at the stop codon found at nucleotide positions 637-639 (Figure 149; SEQ ID NO:221). The predicted polypeptide precursor is 176 amino acids long, has a calculated molecular weight of approximately 19,616 daltons and an estimated pI of approximately 7.11. Analysis of the full-length PRO813 sequence shown in Figure 149 (SEQ ID NO:221) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 26 and potential N-myristoylation sites from about amino acid 48 to about amino acid 53, from about amino acid 153 to about amino acid 158, from about amino acid 156 to about amino acid 161 and from about amino acid 167 to about amino acid 172. Clone DNA57834-1339 has been deposited with the ATCC on June 9, 1998 and is assigned ATCC deposit no. 209954.

Analysis of the amino acid sequence of the full-length PRO813 polypeptide suggests that it possesses sequence similarity to the pulmonary surfactant-associated protein C. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO813 amino acid sequence and the following Dayhoff sequences, P_SPC_MUSVI, P_P91071, G02964, P_R65489, P_P82977, P_R84555, S55542, MUSIGHAJ_1 and PH1158.

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EXAMPLE 64: Isolation of cDNA Clones Encoding Human PRO809

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence. The Incyte EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56418.

In light of an observed sequence homology between the DNA56418 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H74302, the Merck EST clone H74302 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 150 and is herein designated DNA57836-1338.

The entire nucleotide sequence of DNA57836-1338 is shown in Figure 150 (SEQ ID NO:222). Clone DNA57836-1338 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 63-65 and ending at the stop codon at nucleotide positions 858-860 of SEQ ID NO:222 (Figure 150). The predicted polypeptide precursor is 265 amino acids long (Figure 151). The full-length PRO809 protein shown in Figure 151 has an estimated molecular weight of about 29,061 daltons and a pI of about 9.18. Figure 151 further shows the approximate positions of the signal peptide and N-glycosylation sites. The corresponding nucleotides can be determined by referencing Figure 150. Clone DNA57836-1338 has been deposited with ATCC on June 23, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO809 polypeptide suggests that it possesses some sequence similarity to the heparin sulfate proteoglycan and to endothelial cell adhesion molecule-1. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO809 amino acid sequence and the following Dayhoff sequences, PGBM_MOUSE, D82082_1 and PW14158.

EXAMPLE 65: Isolation of cDNA Clones Encoding Human PRO791

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence. The Incyte EST cluster sequence was then compared to a variety of expressed

sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56429.

In light of an observed sequence homology between the DNA56429 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 36367, the Merck EST clone 36367 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 152 and is herein designated DNA57838-1337.

The entire nucleotide sequence of DNA57838-1337 is shown in Figure 152 (SEQ ID NO:224). Clone DNA57838-1337 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 9-11 and ending at the stop codon at nucleotide positions 747-749 of SEQ ID NO:224 (Figure 152). The predicted polypeptide precursor is 246 amino acids long (Figure 153). The full-length PRO791 protein shown in Figure 153 has an estimated molecular weight of about 27,368 daltons and a pI of about 7.45. Figure 153 also shows the approximate locations of the signal peptide, the transmembrane domain, N-glycosylation sites and a region conserved in extracellular proteins. The corresponding nucleotides of one embodiment provided herein can be identified by referencing Figure 152. Clone DNA57838-1337 has been deposited with ATCC on June 23, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO791 polypeptide suggests that it has sequence similarity with MHC-I antigens, thereby indicating that PRO791 may be related to MHC-I antigens. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some sequence identity between the PRO791 amino acid sequence and the following Dayhoff sequences, AF034346_1, MMQ1K5_1 and HFE_HUMAN.

EXAMPLE 66: Isolation of cDNA clones Encoding Human PRO1004

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence, Incyte cluster sequence No. 73681. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated as DNA56516.

In light of an observed sequence homology between the DNA56516 consensus sequence and an EST sequence encompassed within the Merck EST clone no. H43837, the Merck EST clone H43837 was purchased

and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 154.

The full length clone shown in Figure 154 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 119-121 and ending at the stop codon at nucleotide positions 464-466 (Figure 154; SEQ ID NO:226). The predicted polypeptide precursor is 115 amino acids long (Figure 155; SEQ ID NO:227). The full-length PRO1004 protein shown in Figure 155 has an estimated molecular weight of about 13,649 daltons and a pI of about 9.58. Analysis of the full-length PRO1004 sequence shown in Figure 155 (SEQ ID NO:227) evidences the presence of the following features: a signal peptide at about amino acids 1-24, a microbodies C-terminal targeting signal at about amino acids 113-115, a potential N-glycosylation site at about amino acids 71-74, and a domain having sequence identity with dihydrofolate reductase proteins at about amino acids 22-48.

Analysis of the amino acid sequence of the full-length PRO1004 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1004 amino acid sequence and the following Dayhoff sequences: CELR02D3_7, LEC1_MOUSE, AF006691_3, SSZ97390_1, SSZ97395_1, and SSZ97400_1.

Clone DNA57844-1410 was deposited with the ATCC on June 23, 1998, and is assigned ATCC deposit no. 203010.

EXAMPLE 67: Isolation of cDNA clones Encoding Human PRO1111

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which had homology to insulin-like growth factor binding protein.

RNA for construction of cDNA libraries was isolated from human fetal brain. The cDNA libraries used to isolate the cDNA clones encoding human PRO1111 were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI.

The human fetal brain cDNA libraries (prepared as described above), were screened by hybridization with a synthetic oligonucleotide probe based upon the Incyte EST sequence described above:

5'-CCACCACCTGGAGGTCCTGCAGTTGGGCAGGAAGTCCATCCGGCAGATTG-3' (SEQ ID NO:251).

An identified cDNA clone was sequenced in entirety. The entire nucleotide sequence of PRO1111 is shown in Figure 156 (SEQ ID NO:228). Clone DNA58721-1475 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 57-59 and a stop codon at nucleotide positions 2016-2018 (Figure 156; SEQ ID NO:228). The predicted polypeptide precursor is 653 amino acids long (Figure 157). The transmembrane domains are at positions 21-40 (type II) and 528-548. Clone DNA58721-1475 has been deposited with ATCC and is assigned ATCC deposit no. 203110. The full-length PRO1111 protein shown in Figure 157 has an estimated molecular weight of about 72,717 daltons and a pI of about 6.99.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 157 (SEQ ID NO:229), revealed some sequence identity between the PRO1111 amino acid sequence and the following Dayhoff sequences: A58532, D86983_1, RNPLGPV_1, PGS2_HUMAN, AF038127_1, ALS_MOUSE, GPV_HUMAN, PGS2_BOVIN, ALS_PAPPA and I47020.

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EXAMPLE 68: Isolation of cDNA clones Encoding Human PRO1344

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA33790. Based on the DNA33790 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1344.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-AGGTTCTGTGATGGAGACAACCGCG-3' (SEQ ID NO:232)

reverse PCR primer 5'-TGTCAGGACGCACTGCCGTCATG-3' (SEQ ID NO:233)

15 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA33790 sequence which had the following nucleotide sequence

hybridization probe

5'-TGGCCAGATCATCAAGCGTGTCTGTGGCAACGAGCGGCCAGCTCCTATCC-3' (SEQ ID NO:234)

20 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1344 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1344 (designated herein as DNA58723-1588 [Figure 158, SEQ ID NO:230]); and the derived protein sequence for PRO1344.

25 The entire nucleotide sequence of DNA58723-1588 is shown in Figure 158 (SEQ ID NO:230). Clone DNA58723-1588 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 26-28 and ending at the stop codon at nucleotide positions 2186-2188 (Figure 158). The predicted polypeptide precursor is 720 amino acids long (Figure 159). The full-length PRO1344 protein shown in Figure 30 159 has an estimated molecular weight of about 80,199 daltons and a pI of about 7.77. Analysis of the full-length PRO1344 sequence shown in Figure 159 (SEQ ID NO:231) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 23, an EGF-like domain cysteine protein signature sequence from about amino acid 260 to about amino acid 271, potential N-glycosylation sites from about amino acid 96 to about amino acid 99, from about amino acid 279 to about amino acid 282, from about amino acid 316 to about amino acid 319, from about amino acid 451 to about amino acid 454 and from about amino acid 614 to about amino acid 617, an amino acid sequence block having homology to serine proteases, trypsin family from about amino acid 489 to about amino acid 505 and a CUB domain protein profile sequence from about amino

acid 150 to about amino acid 166. Clone DNA58723-1588 has been deposited with ATCC on August 18, 1998 and is assigned ATCC deposit no. 203133.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 159 (SEQ ID NO:231), evidenced significant homology between the PRO1344 amino acid sequence and the following Dayhoff sequences: S77063_1, CRAR_MOUSE, P_R74775, P_P90070, P_R09217, P_P70475, HSBMP16_1 and U50330_1.

EXAMPLE 69: Isolation of cDNA clones Encoding Human PRO1109

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA52642. The consensus DNA sequence was obtained by extending using repeated cycles of BLAST and phrap a previously obtained consensus sequence as far as possible using the sources of EST sequences discussed above. Based on the DNA52642 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1109.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CCTTACCTCAGAGGCCAGAGCAAGC-3' (SEQ ID NO:237)

reverse PCR primer 5'-GAGCTTCATCCGTTCTGCGTTCACC-3' (SEQ ID NO:238)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA52642 sequence which had the following nucleotide sequence

hybridization probe

5'-CAGGAATGTAAAGCTTTACAGAGGGTCGCCATCCTCGTTCCCCACC-3' (SEQ ID NO:239)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1109 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human SK-Lu-1 adenocarcinoma cell tissue (LIB247).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1109 (designated herein as DNA58737-1473 [Figure 160, SEQ ID NO:235]) and the derived protein sequence for PRO1109.

The entire nucleotide sequence of DNA58737-1473 is shown in Figure 160 (SEQ ID NO:235). Clone DNA58737-1473 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 119-120 and ending at the stop codon at nucleotide positions 1151-1153 (Figure 160). The predicted polypeptide precursor is 344 amino acids long (Figure 161). The full-length PRO1109 protein shown in Figure 161 has an estimated molecular weight of about 40,041 daltons and a pI of about 9.34. Analysis of the full-length PRO1109 sequence shown in Figure 161 (SEQ ID NO:236) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 27, potential N-glycosylation sites from about amino acid 4 to about amino acid 7, from about amino acid 220 to about amino acid 223 and from about amino acid 335 to about amino acid 338 and an amino acid sequence block having homology to xylose isomerase proteins from about amino acid 191 to about amino acid 201. Clone DNA58737-1473 has been deposited with ATCC

on August 18, 1998 and is assigned ATCC deposit no. 203136.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 161 (SEQ ID NO:236), evidenced significant homology between the PRO1109 amino acid sequence and the following Dayhoff sequences: HSUDPGAL_1, HSUDPB14_1, NALS_BOVIN, HSU10473_1, CEW02B12_11, YNJ4_CAEEL, AE000738_11, CET24D1_1, S48121 and CEGLY9_1.

EXAMPLE 70: Isolation of cDNA clones Encoding Human PRO1383

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA53961. Based on the DNA53961 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1383.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CATTCCTTACCCTGGACCCAGCTCC-3' (SEQ ID NO:242)

reverse PCR primer 5'-GAAAGGCCACAGCACATCTGGCAG-3' (SEQ ID NO:243)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA53961 sequence which had the following nucleotide sequence

hybridization probe

5'-CCACGACCCGAGCAACTTCCTCAAGACCGACTTGTTTCTCTACAGC-3' (SEQ ID NO:244)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1383 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal brain tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1383 (designated herein as DNA58743-1609 [Figure 162, SEQ ID NO: 240]) and the derived protein sequence for PRO1383.

The entire nucleotide sequence of DNA58743-1609 is shown in Figure 162 (SEQ ID NO:240). Clone DNA58743-1609 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 122-124 and ending at the stop codon at nucleotide positions 1391-1393 (Figure 162). The predicted polypeptide precursor is 423 amino acids long (Figure 163). The full-length PRO1383 protein shown in Figure 163 has an estimated molecular weight of about 46,989 daltons and a pI of about 6.77. Analysis of the full-length PRO1383 sequence shown in Figure 163 (SEQ ID NO:241) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 24, a transmembrane domain from about amino acid 339 to about amino acid 362, and potential N-glycosylation sites from about amino acid 34 to about amino acid 37, from about amino acid 58 to about amino acid 61, from about amino acid 142 to about amino acid 145, from about amino acid 197 to about amino acid 200, from about amino acid 300 to about amino acid 303 and from about amino acid 364 to about amino acid 367. Clone DNA58743-1609 has been deposited with ATCC on

August 25, 1998 and is assigned ATCC deposit no. 203154.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 163 (SEQ ID NO:241), evidenced significant homology between the PRO1383 amino acid sequence and the following Dayhoff sequences: NMB_HUMAN, QNR_COTJA, P_W38335, P115_CHICK, P_W38164, A45993_1, MMU70209_1, D83704_1 and P_W39176.

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EXAMPLE 71: Isolation of cDNA Clones Encoding Human PRO1003

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence designated herein as 43055. This sequence was then compared to a variety of EST databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated consen01.

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2849382, the Incyte EST clone 2849382 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 164.

The entire nucleotide sequence of DNA58846-1409 is shown in Figure 164 (SEQ ID NO:245). Clone DNA58846-1409 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 41-43 and ending at the stop codon at nucleotide positions 293-295 (Figure 164). The predicted polypeptide precursor is 84 amino acids long (Figure 165). The full-length PRO1003 protein shown in Figure 165 has an estimated molecular weight of about 9,408 daltons and a pI of about 9.28. Analysis of the full-length PRO1003 sequence shown in Figure 165 (SEQ ID NO:246) evidences the presence of a signal peptide at amino acids 1 to about 24, and a cAMP- and cGMP-dependent protein kinase phosphorylation site at about amino acids 58 to about 61. Analysis of the amino acid sequence of the full-length PRO1003 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1003 amino acid sequence and the following Dayhoff sequences: AOPCZA363_3, SRTX_ATREN, A48298, MHVJHMS_1, VGL2_CVMJH, DHDHTC2_2, CORT_RAT, TAL6_HUMAN, P_W14123, and DVUFI_2.

EXAMPLE 72: Isolation of cDNA Clones Encoding Human PRO1108

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA53237.

In light of an observed sequence homology between the DNA53237 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2379881, the Incyte EST clone 2379881 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.

The sequence of this cDNA insert is shown in Figure 166 and is herein designated DNA58848-1472.

The entire nucleotide sequence of DNA58848-1472 is shown in Figure 166 (SEQ ID NO:247). Clone DNA58848-1472 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 77-79 and ending at the stop codon at nucleotide positions 1445-1447 (Figure 166). The predicted polypeptide precursor is 456 amino acids long (Figure 167). The full-length PRO1108 protein shown in Figure 167 has an estimated molecular weight of about 52,071 daltons and a pI of about 9.46. Analysis of the full-length PRO1108 sequence shown in Figure 167 (SEQ ID NO:248) evidences the presence of the following: type II transmembrane domains from about amino acid 22 to about amino acid 42, from about amino acid 156 to about amino acid 176, from about amino acid 180 to about amino acid 199 and from about amino acid 369 to about amino acid 388, potential N-glycosylation sites from about amino acid 247 to about amino acid 250, from about amino acid 327 to about amino acid 330, from about amino acid 328 to about amino acid 331 and from about amino acid 362 to about amino acid 365 and an amino acid block having homology to ER lumen protein retaining receptor protein from about amino acid 153 to about amino acid 190. Clone DNA58848-1472 has been deposited with ATCC on June 9, 1998 and is assigned ATCC deposit no. 209955.

Analysis of the amino acid sequence of the full-length PRO1108 polypeptide suggests that it possesses significant sequence similarity to the LPAAT protein, thereby indicating that PRO1108 may be a novel LPAAT homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO1108 amino acid sequence and the following Dayhoff sequences, AF015811_1, CER07E3_2, YL35_CAEEL, S73863, CEF59F4_4, P_W06422, MMU41736_1, MTV008_39, P_R99248 and Y67_BPT7.

EXAMPLE 73: Isolation of cDNA Clones Encoding Human PRO1137

The extracellular domain (ECD) sequences (including the secretion signal, if any) of from about 950 known secreted proteins from the Swiss-Prot public protein database were used to search expressed sequence tag (EST) databases. The EST databases included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)) as a comparison of the ECD protein sequences to a 6 frame translation of the EST sequence. Using this procedure, Incyte EST No. 3459449, also referred to herein as "DNA7108", was identified as an EST having a BLAST score of 70 or greater that did not encode a known protein.

A consensus DNA sequence was assembled relative to the DNA7108 sequence and other ESTs using repeated cycles of BLAST and the program "phrap" (Phil Green, Univ. of Washington, Seattle, WA). The consensus sequence obtained therefrom is referred to herein as DNA53952.

In light of an observed sequence homology between the DNA53952 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3663102, the Incyte EST clone 3663102 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 168.

The entire nucleotide sequence of DNA58849-1494 is shown in Figure 168 (SEQ ID NO:249). Clone DNA58849-1494 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 77-79 and ending at the stop codon at nucleotide positions 797-799 (Figure 168). The predicted polypeptide precursor is 240 amino acids long (Figure 169). The full-length PRO1137 protein shown in Figure 169 has an estimated molecular weight of about 26,064 daltons and a pI of about 8.65. Analysis of the full-length PRO1137 sequence shown in Figure 169 (SEQ ID NO:250) evidences the presence of a signal peptide at about amino acids 1 to 14 and a potential N-glycosylation site at about amino acids 101-105.

Analysis of the amino acid sequence of the full-length PRO1137 polypeptide suggests that it possesses significant sequence similarity to ribosyltransferase thereby indicating that PRO1137 may be a novel member of the ribosyltransferase family of proteins. Analysis of the amino acid sequence of the full-length PRO1137 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1137 amino acid sequence and the following Dayhoff sequences: MMART5_1, NARG_MOUSE, GEN11909, GEN13794, GEN14406, MMRNART62_1, and P_R41876.

EXAMPLE 74: Isolation of cDNA clones Encoding Human PRO1138

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence, Incyte cluster sequence no. 165212. This cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated as DNA54224. The assembly included a proprietary Genentech EST designated herein as DNA49140 (Figure 172; SEQ ID NO:254).

In light of an observed sequence homology between the DNA54224 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3836613, the Incyte EST clone 3836613 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 170 and is the full-length DNA sequence for PRO1138. Clone DNA58850-1495 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209956.

The entire nucleotide sequence of DNA58850-1495 is shown in Figure 170 (SEQ ID NO:252). Clone DNA58850-1495 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 38-40 and ending at the stop codon at nucleotide positions 1043-1045 (Figure 170). The predicted polypeptide precursor is 335 amino acids long (Figure 171). The full-length PRO1138 protein shown in Figure 171 has an estimated molecular weight of about 37,421 Daltons and a pI of about 6.36. Analysis of the full-length PRO1138 sequence shown in Figure 171 (SEQ ID NO:253) evidences the presence of the following features: a signal peptide at about amino acid 1 to about amino acid 22; a transmembrane domain at about amino

acids 224 to about 250; a leucine zipper pattern at about amino acids 229 to about 250; and potential N-glycosylation sites at about amino acids 98-101, 142-145, 148-151, 172-175, 176-179, 204-207, and 291-295.

Analysis of the amino acid sequence of the full-length PRO1138 polypeptide suggests that it possesses significant sequence similarity to the CD84, thereby indicating that PRO1138 may be a novel member of the Ig superfamily of polypeptides. More particularly, analysis of the amino acid sequence of the full-length PRO1138 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1138 amino acid sequence and the following Dayhoff sequences: HSU82988_1, HUMLY9_1, P_R97631, P_R97628, P_R97629, P_R97630, CD48_RAT, CD2_HUMAN, P_P93996, and HUMBGP_1.

Clone DNA58850-1495 was deposited with ATCC on June 9, 1998, and is assigned ATCC deposit no. 209956.

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EXAMPLE 75: Isolation of cDNA clones Encoding Human PRO1054

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 66212. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55722.

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In light of an observed sequence homology between the DNA55722 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 319751, the Incyte EST clone 319751 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 173 and is herein designated as DNA58853-1423.

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Clone DNA58853-1423 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 46-48 and ending at the stop codon at nucleotide positions 586-588 (Figure 173). The predicted polypeptide precursor is 180 amino acids long (Figure 174). The full-length PRO1054 protein shown in Figure 174 has an estimated molecular weight of about 20,638 daltons and a pI of about 5.0. Analysis of the full-length PRO1054 sequence shown in Figure 174 (SEQ ID NO:256) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 18, a leucine zipper pattern from about amino acid 155 to about amino acid 176 and amino acid sequence blocks having homology to lipocalin proteins from about amino acid 27 to about amino acid 38 and from about amino acid 110 to about amino acid 120. Clone DNA58853-1423 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203016.

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An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 174 (SEQ ID NO:256), evidenced significant homology between the PRO1054 amino acid sequence and the following Dayhoff sequences: MUP1_MOUSE, MUP6_MOUSE, MUP2_MOUSE, MUP8_MOUSE, MUP5_MOUSE, MUP4_MOUSE, S10124,

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MUPM_MOUSE, MUP_RAT and ECU70823_1.

EXAMPLE 76: Isolation of cDNA clones Encoding Human PRO994

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 157555. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55728.

In light of an observed sequence homology between the DNA55728 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2860366, the Incyte EST clone 2860366 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 175 and is herein designated as DNA58855-1422.

Clone DNA58855-1422 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 31-33 and ending at the stop codon at nucleotide positions 718-720 (Figure 175). The predicted polypeptide precursor is 229 amino acids long (Figure 176). The full-length PRO994 protein shown in Figure 176 has an estimated molecular weight of about 25,109 daltons and a pI of about 6.83. Analysis of the full-length PRO994 sequence shown in Figure 176 (SEQ ID NO:258) evidences the presence of the following: transmembrane domains from about amino acid 10 to about amino acid 31, from about amino acid 50 to about amino acid 72, from about amino acid 87 to about amino acid 110 and from about amino acid 191 to about amino acid 213, potential N-glycosylation sites from about amino acid 80 to about amino acid 83, from about amino acid 132 to about amino acid 135, from about amino acid 148 to about amino acid 151 and from about amino acid 163 to about amino acid 166 and an amino acid block having homology to TNFR/NGFR cysteine-rich region proteins from about amino acid 4 to about amino acid 11. Clone DNA58855-1422 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203018.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 176 (SEQ ID NO:258), evidenced significant homology between the PRO994 amino acid sequence and the following Dayhoff sequences: AF027204_1, TAL6_HUMAN, ILT4_HUMAN, JC6205, MMU57570_1, S40363, ETU56093_1, S42858, P_R66849 and P_R74751.

EXAMPLE 77: Isolation of cDNA clones Encoding Human PRO812

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 170079. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank)

and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated as DNA55721.

In light of an observed sequence homology between the DNA55721 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 388964, the Incyte EST clone 388964 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 177 and is herein designated as DNA59205-1421.

Clone DNA59205-1421 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 55-57 and ending at the stop codon at nucleotide positions 304-306 (Figure 177). The predicted polypeptide precursor is 83 amino acids long (Figure 178). The full-length PRO812 protein shown in Figure 178 has an estimated molecular weight of about 9,201 daltons and a pI of about 9.3. Analysis of the full-length PRO812 sequence shown in Figure 178 (SEQ ID NO:260) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15, a cAMP- and cGMP-dependent protein kinase phosphorylation site from about amino acid 73 to about amino acid 76 and protein kinase C phosphorylation sites from about amino acid 70 to about amino acid 72 and from about amino acid 76 to about amino acid 78. Clone DNA59205-1421 has been deposited with ATCC on June 23, 1998 and is assigned ATCC deposit no. 203009.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 178 (SEQ ID NO:260), evidenced significant homology between the PRO812 amino acid sequence and the following Dayhoff sequences: P_W35802, P_W35803, PSC1_RAT, S68231, GEN13917, PSC2_RAT, CC10_HUMAN, UTER_RABBIT, AF008595_1 and A56413.

25 EXAMPLE 78: Isolation of cDNA clones Encoding Human PRO1069

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence designated herein as 100727. This sequence was then compared to a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56001.

In light of an observed sequence homology between the DNA56001 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3533881, the Incyte EST clone 3533881 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 179 and is the full-length DNA sequence for PRO1069.

Clone DNA59211-1450 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209960.

The entire nucleotide sequence of DNA59211-1450 is shown in Figure 179 (SEQ ID NO:261). Clone DNA59211-1450 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 197-199 and ending at the stop codon at nucleotide positions 464-466. The predicted polypeptide precursor is 89 amino acids long (Figure 180). The full-length PRO1069 protein shown in Figure 180 has an estimated molecular weight of about 9,433 daltons and a pI of about 8.21. Analysis of the full-length PRO1069 sequence shown in Figure 180 (SEQ ID NO:262) evidences the presence of the following features: a signal peptide sequence at amino acid 1 to about 16; a transmembrane domain at about amino acids 36 to about 59; potential N-myristoylation sites at about amino acids 41-46, 45-50, and 84-89; and homology with extracellular proteins SCP/Tpx-1/Ag5/PR-1/Sc7 at about amino acids 54 to about 66.

Analysis of the amino acid sequence of the full-length PRO1069 polypeptide suggests that it possesses significant sequence similarity to CHIF, thereby indicating that PRO1069 may be a member of the CHIF family of polypeptides. More particularly, analysis of the amino acid sequence of the full-length PRO1069 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1069 amino acid sequence and the following Dayhoff sequences: CHIF_RAT, A55571, PLM_HUMAN, A40533, ATNG_BOVIN, RIC_MOUSE, PETD_SYNY3, VTB1_XENLA, A05009, and S75086.

Clone DNA59211-1450 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209960.

20 EXAMPLE 79: Isolation of cDNA Clones Encoding Human PRO1129

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence designated herein as 98833. The Incyte EST cluster sequence no. 98833 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56038.

30 In light of an observed sequence homology between the DNA56038 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1335241, the Incyte EST clone 1335241 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 181 and is herein designated DNA59213-1487.

35 The full length clone shown in Figure 181 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 42-44 and ending at the stop codon found at nucleotide positions 1614-1616 (Figure 181; SEQ ID NO:263). The predicted polypeptide precursor is 524 amino acids long, has a calculated molecular weight of approximately 60,310 daltons and an estimated pI of approximately 7.46.

Analysis of the full-length PRO1129 sequence shown in Figure 182 (SEQ ID NO:264) evidences the presence of the following: type II transmembrane domains from about amino acid 13 to about amino acid 32 and from about amino acid 77 to about amino acid 102, a cytochrome P-450 cysteine heme-iron ligand signature sequence from about amino acid 461 to about amino acid 470 and potential N-glycosylation sites from about amino acid 112 to about amino acid 115 and from about amino acid 168 to about amino acid 171. Clone DNA59213-1487
 5 has been deposited with the ATCC on June 9, 1998 and is assigned ATCC deposit no. 209959.

Analysis of the amino acid sequence of the full-length PRO1129 polypeptide suggests that it possesses sequence similarity to the cytochrome P-450 family of proteins. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO1129 amino acid sequence and the following Dayhoff sequences, AC004523_1, S45702, AF054821_1 and I53015.

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EXAMPLE 80: Isolation of cDNA clones Encoding Human PRO1068

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the LIFESEQ® database, designated Incyte cluster no. 141736. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. One or more of the ESTs was derived from a human mast cell line from a patient with mast cell leukemia. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56094.
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In light of an observed sequence homology between the DNA56094 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 004974, the Incyte EST clone 004974 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.
 25 The sequence of this cDNA insert is shown in Figure 183 and is herein designated as DNA59214-1449 (SEQ ID NO:265).

The full length clone shown in Figure 183 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 42-44 and ending at the stop codon found at nucleotide positions 414-416 (Figure 183; SEQ ID NO:265). The predicted polypeptide precursor (Figure 184, SEQ ID NO:266) is 124 amino acids long. PRO1068 has a calculated molecular weight of approximately 14,284 daltons and an estimated pI of approximately 8.14. The PRO1068 polypeptide has the following additional features, as indicated in Figure 184: a signal peptide sequence at about amino acids 1-20, a urotensin II signature sequence at about amino acids 118-123, a cell attachment sequence at about amino acids 64-66, and a potential cAMP- and cGMP-dependent protein kinase phosphorylation site at about amino acids 112-115.
 30

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 184 (SEQ ID NO:266), revealed homology between the PRO1068 amino acid sequence and the following Dayhoff sequences: HALBOP_1, MTV043_36,
 35

150498, and P_R78445

Clone DNA59214-1449 was deposited with the ATCC on July 1, 1998 and is assigned ATCC deposit no.203046.

EXAMPLE 81: Isolation of cDNA clones Encoding Human PRO1066

5 Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST cluster sequence designated herein as 79066. The Incyte EST cluster sequence no. 79066 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or
10 BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56121.

In light of an observed sequence homology between the DNA56121 consensus sequence and an EST
15 sequence encompassed within the Incyte EST clone no. 1515315, the Incyte EST clone 1515315 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 185 and is herein designated DNA59215-1425.

The full length clone shown in Figure 185 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 176-178 and ending at the stop codon found at nucleotide
20 positions 527-529 (Figure 185; SEQ ID NO:267). The predicted polypeptide precursor is 117 amino acids long, has a calculated molecular weight of approximately 12,911 daltons and an estimated pI of approximately 5.46. Analysis of the full-length PRO1066 sequence shown in Figure 186 (SEQ ID NO:268) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 23, a cAMP- and cGMP-dependent protein kinase phosphorylation site from about amino acid 38 to about amino acid 41 and potential
25 N-myristoylation sites from about amino acid 5 to about amino acid 10, from about amino acid 63 to about amino acid 68 and from about amino acid 83 to about amino acid 88. Clone UNQ524 (DNA59215-1425) has been deposited with the ATCC on June 9, 1998 and is assigned ATCC deposit no. 209961.

Analysis of the amino acid sequence of the full-length PRO1066 polypeptide suggests that it does not possess significant sequence similarity to any known human protein. However, an analysis of the Dayhoff
30 database (version 35.45 SwissProt 35) evidenced some degree of homology between the PRO1066 amino acid sequence and the following Dayhoff sequences, MOTI_HUMAN, AF025667_1, MTCY19H9_8 and RABIGKCH_1.

EXAMPLE 82: Isolation of cDNA Clones Encoding Human PRO1184

35 Use of the signal sequence algorithm described in Example 3 on ESTs from an Incyte database allowed identification a candidate sequence designated herein as DNA56375. This sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and

a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56375.

In light of an observed sequence homology between the DNA56375 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1428374, the Incyte EST clone 1428374 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 187.

The full length clone shown in Figure 187 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 106-108 and ending at the stop codon found at nucleotide positions 532-534 (Figure 187; SEQ ID NO:269). The predicted polypeptide precursor is 142 amino acids long, has a calculated molecular weight of approximately 15,690 daltons and an estimated pI of approximately 9.64. Analysis of the full-length PRO1184 sequence shown in Figure 188 (SEQ ID NO:270) evidences the presence of a signal peptide at about amino acids 1-38. Clone DNA59220-1514 has been deposited with the ATCC on June 9, 1998. It is understood that the deposited clone has the actual sequences and that representations are presented herein.

Analysis of the amino acid sequence of the full-length PRO1184 polypeptide suggests that it possesses some sequence identity with a protein called TIM from *Drosophila virilis*, designated "DVTIMS02_1" in the Dayhoff data base, (version 35.45 SwissProt 35). Other Dayhoff database (version 35.45 SwissProt 35) sequences having some degree of sequence identity with PRO1184 include: WIS1_SCHPO, F002186_1, ATAC00239124 and MSAIPRP_1.

EXAMPLE 83: Isolation of cDNA clones Encoding Human PRO1360

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST sequence from an Incyte database, designated DNA10572. This EST sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank, Merck/Wash. U.) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57314.

In light of an observed sequence homology between the DNA57314 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA406443, the Merck EST clone AA406443 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 189 and is herein designated as DNA59488-1603.

The full length clone shown in Figure 189 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 54-56 and ending at the stop codon found at nucleotide positions 909-911 (Figure 189; SEQ ID NO:271). The predicted polypeptide precursor (Figure 190, SEQ ID NO:272) is 285 amino acids long. PRO1360 has a calculated molecular weight of approximately 31,433 daltons and an estimated pI of approximately 7.32. Clone DNA59488-1603 was deposited with the ATCC on August 25, 1998 and is assigned ATCC deposit no. 203157.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 190 (SEQ ID NO:272), revealed sequence identity between the PRO1360 amino acid sequence and the following Dayhoff sequences: UN51_CAEEL, YD4B_SCHPO, AF000634_1, GFO_ZYMMO, YE1J_SCHPO, D86566_1, ZMGFO_1, S76976, PPSA_SYNY3, and CEF28B1_4.

EXAMPLE 84: Isolation of cDNA clones Encoding Human PRO1029

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 18763. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57854.

In light of an observed sequence homology between the DNA57854 consensus sequence and an EST sequence encompassed within the Merck EST clone no. T98880, the Merck EST clone T98880 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 191 and is herein designated as DNA59493-1420.

Clone DNA59493-1420 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 39-41 and ending at the stop codon at nucleotide positions 297-299 (Figure 191). The predicted polypeptide precursor is 86 amino acids long (Figure 192). The full-length PRO1029 protein shown in Figure 192 has an estimated molecular weight of about 9,548 daltons and a pI of about 8.52. Analysis of the full-length PRO1029 sequence shown in Figure 192 (SEQ ID NO:274) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19, an amino acid block having homology to bacterial rhodopsins retinal binding site protein from about amino acid 50 to about amino acid 61, a prenyl group binding site from about amino acid 83 to about amino acid 86 and a potential N-glycosylation site from about amino acid 45 to about amino acid 48. Clone DNA59493-1420 has been deposited with ATCC on July 1, 1998 and is assigned ATCC deposit no. 203050.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 192 (SEQ ID NO:274), evidenced significant

homology between the PRO1029 amino acid sequence and the following Dayhoff sequences: S66088, AF031815_1, MM4A6L_1, PSEIS52a-1, S17699 and P_R63635.

EXAMPLE 85: Isolation of cDNA clones Encoding Human PRO1139

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 4461. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57312.

The DNA57312 consensus sequence included a 172 nucleotides long public EST (T62095, Merck/University of Washington public database). This EST clone, identified herein as a putative protein coding sequence, was purchased from Merck, and sequenced to provide the coding sequence of PRO1139 (Figure 193). As noted before, the deduced amino acid sequence of DNA59497-1496 shows a significant sequence identity with the deduced amino acid sequence of HSOBRGRP_1. The full-length protein (Figure 194) contains a putative signal peptide between amino acid residues 1 and about 28, and three putative transmembrane domains (approximate amino acid residues 33-52, 71-89, 98-120).

EXAMPLE 86: Isolation of cDNA clones Encoding Human PRO1309

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed homology to SLIT.

RNA for construction of cDNA libraries was isolated from human fetal brain tissue. The cDNA libraries used to isolate the cDNA clones encoding human PRO1309 were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI.

The cDNA libraries (prepared as described above), were screened by hybridization with a synthetic oligonucleotide probe derived from the above described Incyte EST sequence:

5'-TCCGTGCAGGGGACGCCTTTCAGAACTGCGCCGAGTTAAGGAAC-3' (SEQ ID NO:279).

A cDNA clone was isolated and sequenced in entirety. The entire nucleotide sequence of DNA59588-1571 is shown in Figure 195 (SEQ ID NO:277). Clone DNA59588-1571 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 720-722 and a stop codon at nucleotide positions 2286-2288 (Figure 195; SEQ ID NO:277). The predicted polypeptide precursor is 522 amino acids

long. The signal peptide is approximately at 1-34 and the transmembrane domain is at approximately 428-450 of SEQ ID NO:278. Clone DNA59588-1571 has been deposited with ATCC and is assigned ATCC deposit no. 203106. The full-length PRO1309 protein shown in Figure 196 has an estimated molecular weight of about 58,614 daltons and a pI of about 7.42.

- 5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 196 (SEQ ID NO:278), revealed sequence identity between the PRO1309 amino acid sequence and the following Dayhoff sequences: AB007876_1, GPV_MOUSE, ALS_RAT, P_R85889, LUM_CHICK, AB014462_1, PGS1_CANFA, CEM88_7, A58532 and GEN11209.

EXAMPLE 87: Isolation of cDNA Clones Encoding Human PRO1028

- 10 Use of the signal sequence algorithm described in Example 3 above allowed identification of a certain EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in
15 Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA59603.

- 20 In light of an observed sequence homology between the DNA59603 sequence and an EST sequence contained within Incyte EST clone no. 1497725, the Incyte EST clone no. 1497725 was purchased and the cDNA insert was obtained and sequenced. It was found that the insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 197 and is herein designated as DNA59603-1419.

- 25 The entire nucleotide sequence of DNA59603-1419 is shown in Figure 197 (SEQ ID NO:280). Clone DNA59603-1419 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 21-23 and ending at the stop codon at nucleotide positions 612-614 (Figure 197). The predicted polypeptide precursor is 197 amino acids long (Figure 198). The full-length PRO1028 protein shown in Figure 198 has an estimated molecular weight of about 20,832 daltons and a pI of about 8.74. Clone DNA59603-1419 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains the correct sequence, and the sequences provided herein are based on known sequencing techniques.

- 30 Analyzing the amino acid sequence of SEQ ID NO:281, the putative signal peptide is at about amino acids 1-19 of SEQ ID NO:281. An N-glycosylation site is at about amino acids 35-38 of SEQ ID NO:281. A C-type lectin domain is at about amino acids 108-117 of SEQ ID NO:281, indicating that PRO513 may be related to or be a lectin. The corresponding nucleotides of these amino acid sequences or others can be routinely determined given the sequences provided herein.

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EXAMPLE 88: Isolation of cDNA Clones Encoding Human PRO1027

Use of the signal sequence algorithm described in Example 3 above allowed identification of a certain EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ[®], Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The

5 homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56399.

10 In light of an observed sequence homology between the DNA56399 sequence and an EST sequence contained within Incyte EST clone no. 937605, the Incyte EST clone no. 937605 was purchased and the cDNA insert was obtained and sequenced. It was found that the insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 199 and is herein designated as DNA59605-1418.

The entire nucleotide sequence of DNA59605-1418 is shown in Figure 199 (SEQ ID NO:282). Clone

15 DNA59605-1418 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 31-33 and ending at the stop codon at nucleotide positions 262-264 (Figure 199). The predicted polypeptide precursor is 77 amino acids long (Figure 200). The full-length PRO1027 protein shown in Figure 200 has an estimated molecular weight of about 8,772 daltons and a pI of about 9.62. Clone DNA59605-1418 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains

20 the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:283, the putative signal peptide is at about amino acids 1-33 of SEQ ID NO:283. The type II fibronectin collagen-binding domain begins at about amino acid 30 of SEQ ID NO:283. The corresponding nucleotides for these amino acid sequences and others can be routinely determined given the sequences provided herein. PRO1027 may be involved in tissue formation or repair.

25 The following Dayhoff designations appear to have some sequence identity with PRO1027: SFT2_YEAST; ATM3E9_2; A69826; YM16_MARPO; E64896; U60193_2; MTLRAJ205_1; MCU60315_70; SPAS_SHIFL; and S54213.

EXAMPLE 89: Isolation of cDNA Clones Encoding Human PRO1107

30 Use of the signal sequence algorithm described in Example 3 above allowed identification of a certain EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ[®], Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The

homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence

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obtained therefrom is herein designated DNA56402.

In light of an observed sequence homology between the DNA56402 sequence and an EST sequence contained within Incyte EST clone no. 3203694, the Incyte EST clone no. 3203694 was purchased and the cDNA insert was obtained and sequenced. It was found that the insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 201 and is herein designated as DNA59606-1471.

- 5 The entire nucleotide sequence of DNA59606-1471 is shown in Figure 201 (SEQ ID NO:284). Clone DNA59606-1471 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 244-246 and ending at the stop codon at nucleotide positions 1675-1677 of SEQ ID NO:284 (Figure 201). The predicted polypeptide precursor is 477 amino acids long (Figure 202). The full-length PRO1107 protein shown in Figure 202 has an estimated molecular weight of about 54,668 daltons and a pI of about 6.33.
- 10 Clone DNA59606-1471 has been deposited with ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

- Analysis of the amino acid sequence of the full-length PRO1107 polypeptide suggests that it possesses significant sequence similarity to phosphodiesterase I/nucleotide pyrophosphatase, human insulin receptor tyrosine kinase inhibitor, alkaline phosphodiesterase and autotaxin, thereby indicating that PRO1107 may have at least one or all of the activities of these proteins, and that PRO1107 is a novel phosphodiesterase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO1107 amino acid sequence and at least the following Dayhoff sequences: AF005632_1, P_R79148, RNU78787_1, AF060218_4, A57080 and HUMATXT_1.
- 15

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EXAMPLE 90: Isolation of cDNA clones Encoding Human PRO1140

- Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence, Incyte cluster sequence No. 135917. This sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary
- 25 EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained
- 30 therefrom is herein designated DNA56416.

- In light of an observed sequence homology between DNA56416 and an EST sequence contained within Incyte EST clone no. 3345705, Incyte EST clone no. 3345705 was obtained and its insert sequenced. It was found that the insert encoded a full-length protein. The sequence, designated herein as DNA59607-1497, which is shown in Figure 203, is the full-length DNA sequence for PRO1140. Clone DNA59607-1497 was deposited
- 35 with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209946.

The entire nucleotide sequence of DNA59607-1497 is shown in Figure 203 (SEQ ID NO:286). Clone DNA59607-1497 contains a single open reading frame with an apparent translational initiation site at nucleotide

positions 210-212 and ending at the stop codon at nucleotide positions 975-977 (Figure 203). The predicted polypeptide precursor is 255 amino acids long (Figure 204). The full-length PRO1140 protein shown in Figure 204 has an estimated molecular weight of about 29,405 daltons and a pI of about 7.64. Analysis of the full-length PRO1140 sequence shown in Figure 204 (SEQ ID NO:287) evidences the presence of three transmembrane domains at about amino acids 101 to 118, 141 to 161 and 172 to 191.

5 Analysis of the amino acid sequence of the full-length PRO1140 polypeptide using the Dayhoff database (version 35.45 SwissProt 35) evidenced homology between the PRO1140 amino acid sequence and the following Dayhoff sequences: AF023602_1, AF000368_1, CIN3_RAT, AF003373_1, GEN13279, and AF003372_1.

Clone DNA59607-1497 was deposited with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209946.

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EXAMPLE 91: Isolation of cDNA clones Encoding Human PRO1106

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single Incyte EST sequence. This sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using
15 the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, Univ. of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated
20 DNA56423.

In light of an observed sequence homology between DNA56423 and an EST sequence contained within Incyte EST clone no. 1711247, Incyte EST clone no. 1711247 was obtained and its insert sequenced. It was found that the insert encoded a full-length protein. The sequence, designated herein as DNA59609-1470, which is shown in Figure 205, is the full-length DNA sequence for PRO1106. Clone DNA59609-1470 was deposited
25 with the ATCC on June 9, 1998, and is assigned ATCC deposit no. 209963.

The entire nucleotide sequence of DNA59609-1470 is shown in Figure 205 (SEQ ID NO:288). Clone DNA59609-1470 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 61-63 and ending at the stop codon at nucleotide positions 1468-1470 of SEQ ID NO:288 (Figure 205). The predicted polypeptide precursor is 469 amino acids long (Figure 206). The full-length PRO1106 protein
30 shown in Figure 206 has an estimated molecular weight of about 52,689 daltons and a pI of about 8.68. It is understood that the skilled artisan can construct the polypeptide or nucleic acid encoding therefor to exclude any one or more of all of these domains. For example, the transmembrane domain region(s) and/or either of the amino terminal or carboxyl end can be excluded. Clone DNA59609-1470 has been deposited with ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the
35 sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO1106 polypeptide suggests that it possesses significant sequence similarity to the peroxisomal ca-dependent solute carrier, thereby indicating that PRO1106

may be a novel transporter. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO1106 amino acid sequence and at least the following Dayhoff sequences, AF004161_1, IG002N01_25, GDC_BOVIN and BT1_MAIZE.

EXAMPLE 92: Isolation of cDNA clones Encoding Human PRO1291

5 Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 120480. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul
10 et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56425.

15 In light of an observed sequence homology between the DNA56425 sequence and an EST sequence encompassed within the Incyte EST clone no. 2798803, the Incyte EST clone 2798803 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 207 and is herein designated as DNA59610-1556.

20 Clone DNA59610-1556 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 61-63 and ending at the stop codon at nucleotide positions 907-909 (Figure 207). The predicted polypeptide precursor is 282 amino acids long (Figure 208). The full-length PRO1291 protein shown in Figure 208 has an estimated molecular weight of about 30,878 daltons and a pI of about 5.27. Analysis of the full-length PRO1291 sequence shown in Figure 208 (SEQ ID NO:291) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, a transmembrane domain from about amino acid 258 to about amino acid 281 and potential N-glycosylation sites from about amino acid 112 to about
25 amino acid 115, from about amino acid 160 to about amino acid 163, from about amino acid 190 to about amino acid 193, from about amino acid 196 to about amino acid 199, from about amino acid 205 to about amino acid 208, from about amino acid 216 to about amino acid 219 and from about amino acid 220 to about amino acid 223.. Clone DNA59610-1556 has been deposited with ATCC on June 16, 1998 and is assigned ATCC deposit no. 209990.

30 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 208 (SEQ ID NO:291), evidenced significant homology between the PRO1291 amino acid sequence and the following Dayhoff sequences: HSU90552_1, HSU90144_1, AF033107_1, HSB73_1, HSU90142_1, GGCD80_1, P_W34452, MOG_MOUSE, B39371 and P_R71360.

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EXAMPLE 93: Isolation of cDNA clones Encoding Human PRO1105

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56430.

In light of an observed sequence homology between the DNA56430 sequence and an EST sequence encompassed within the Incyte EST clone no. 1853047, the Incyte EST clone 1853047 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 209 and is herein designated as DNA59612-1466.

The entire nucleotide sequence of DNA59612-1466 is shown in Figure 209 (SEQ ID NO:292). Clone DNA59612-1466 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 28-30 and ending at the stop codon at nucleotide positions 568-570 of SEQ ID NO:292 (Figure 209). The predicted polypeptide precursor is 180 amino acids long (Figure 210). The full-length PRO1105 protein shown in Figure 210 has an estimated molecular weight of about 20,040 daltons and a pI of about 8.35. Clone DNA59612-1466 has been deposited with the ATCC on June 9, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analyzing Figure 210, a signal peptide is at about amino acids 1-19 of SEQ ID NO:293 and transmembrane domains are shown at about amino acids 80-99 and 145-162 of SEQ ID NO:293. It is understood that the skilled artisan could form a polypeptide with all of or any combination or individual selection of these regions. It is also understood that the corresponding nucleic acids can be routinely identified and prepared based on the information provided herein.

EXAMPLE 94: Isolation of cDNA clones Encoding Human PRO511

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56434.

In light of an observed sequence homology between the DNA56434 sequence and an EST sequence encompassed within the Incyte EST clone no. 1227491, the Incyte EST clone 1227491 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 211 and is herein designated as DNA59613-1417.

The entire nucleotide sequence of DNA59613-1417 is shown in Figure 211 (SEQ ID NO:294). Clone
 5 DNA59613-1417 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 233-235 and ending at the stop codon at nucleotide positions 944-946 (Figure 211). The predicted polypeptide precursor is 237 amino acids long (Figure 212). The full-length PRO511 protein shown in Figure 212 has an estimated molecular weight of about 25,284 daltons and a pI of about 5.74. Clone DNA59613-1417 has been deposited with the ATCC. Regarding the sequence, it is understood that the deposited clone contains
 10 the correct sequence, and the sequences provided herein are based on known sequencing techniques.

Analyzing the amino acid sequence of SEQ ID NO:295, the putative signal peptide is at about amino acids 1-25 of SEQ ID NO:295. The N-glycosylation sites are at about amino acids 45-48, 73-76, 107-110, 118-121, 132-135, 172-175, 175-178 and 185-188 of SEQ ID NO:295. An arthropod defensins conserved region is at about amino acids 176-182 of SEQ ID NO:295. A kringle domain begins at about amino acid 128 of SEQ
 15 ID NO:295 and a ly-6/u-PAR domain begins at about amino acid 6 of SEQ ID NO:295. The corresponding nucleotides of these amino acid sequences and others can be routinely determined given the sequences provided herein.

The designations appearing in a Dayhoff database with which PRO511 has some sequence identity are as follows: SSC20F10_1; SF041083; P_W26579; S44208; JC2394; PSTA_DICDI; A27020; S59310;
 20 RAG1_RABIT; and MUSBALBC1_1.

EXAMPLE 95: Isolation of cDNA clones Encoding Human PRO1104

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of
 25 expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with
 30 the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56446.

In light of an observed sequence homology between the DNA56446 sequence and an EST sequence encompassed within the Incyte EST clone no. 2837496, the Incyte EST clone 2837496 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The
 35 sequence of this cDNA insert is shown in Figure 213 and is herein designated as DNA59616-1465.

The entire nucleotide sequence of DNA59616-1465 is shown in Figure 213 (SEQ ID NO:296). Clone DNA59616-1465 contains a single open reading frame with an apparent translational initiation site at nucleotide

positions 109-111 and ending at the stop codon at nucleotide positions 1132-1134 of SEQ ID NO:296 (Figure 213). The predicted polypeptide precursor is 341 amino acids long (Figure 214). The full-length PRO1104 protein shown in Figure 214 has an estimated molecular weight of about 36,769 daltons and a pI of about 9.03. Clone DNA59616-1465 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analyzing Figure 214, a signal peptide is at about amino acids 1-22 of SEQ ID NO:297. N-myristoylation sites are at about amino acids 41-46, 110-115, 133-138, 167-172 and 179-184 of SEQ ID NO:297.

10 EXAMPLE 96: Isolation of cDNA clones Encoding Human PRO1100

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

In light of an observed sequence homology between the obtained consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2305379, the Incyte EST clone 2305379 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 215 and is herein designated as DNA59619-1464.

The entire nucleotide sequence of DNA59619-1464 is shown in Figure 215 (SEQ ID NO:298). Clone DNA59619-1464 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 33-35 and ending at the stop codon at nucleotide positions 993-995 of SEQ ID NO:298 (Figure 215). The predicted polypeptide precursor is 320 amino acids long (Figure 216). The full-length PRO1100 protein shown in Figure 216 has an estimated molecular weight of about 36,475 daltons and a pI of about 7.29. Clone DNA59619-1464 has been deposited with ATCC on July 1, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Upon analyzing SEQ ID NO:299, the approximate locations of the signal peptide, the transmembrane domains, an N-glycosylation site, an N-myristoylation site, a CUB domain and an amiloride-sensitive sodium channel domain are present. It is believed that PRO1100 may function as a channel. The corresponding nucleic acids for these amino acids and others can be routinely determined given SEQ ID NO:299..

EXAMPLE 97: Isolation of cDNA clones Encoding Human PRO836

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (Lifeseq®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The
5 homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained is herein designated DNA56453.

10 In light of an observed sequence homology between the DNA56453 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2610075, the Incyte EST clone 2610075 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 217 and is herein designated as DNA59620-1463.

The entire nucleotide sequence of DNA59620-1463 is shown in Figure 217 (SEQ ID NO:300). Clone
15 DNA59620-1463 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 65-67 and ending at the stop codon at nucleotide positions 1448-1450 of SEQ ID NO:300 (Figure 217). The predicted polypeptide precursor is 461 amino acids long (Figure 218). The full-length PRO836 protein shown in Figure 218 has an estimated molecular weight of about 52,085 daltons and a pI of about 5.36. Analysis of the full-length PRO836 sequence shown in Figure 218 (SEQ ID NO:301) evidences the presence of the
20 following: a signal peptide, N-glycosylation sites, N-myristoylation sites, a domain conserved in the YJL126w/YLR351c/yhcX family of proteins, and a region having sequence identity with SLS1. Clone DNA59620-1463 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

25 Analysis of the amino acid sequence of the full-length PRO836 polypeptide suggests that it possesses some sequence similarity to SLS1, thereby indicating that PRO836 may be involved in protein translocation of the ER. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced some homology between the PRO836 amino acid sequence and at least the following Dayhoff sequences, S58132, SPBC3B9_1, S66714, CRU40057_1 and IMA_CAEEL.

30

EXAMPLE 98: Isolation of cDNA clones Encoding Human PRO1141

Use of the signal sequence algorithm described in Example 3 above allowed identification of an EST cluster sequence from the Incyte database, designated 11873. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank)
35 and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or

in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56518.

In light of an observed sequence homology between the DNA56518 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2679995, the Incyte EST clone 2679995 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 219 and is herein designated as DNA59625-1498.

Clone DNA59625-1498 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 204-206 and ending at the stop codon at nucleotide positions 945-947 (Figure 219). The predicted polypeptide precursor is 247 amino acids long (Figure 220). The full-length PRO1141 protein shown in Figure 220 has an estimated molecular weight of about 26,840 daltons and a pI of about 8.19. Analysis of the full-length PRO1141 sequence shown in Figure 220 (SEQ ID NO:303) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19 and transmembrane domains from about amino acid 38 to about amino acid 57, from about amino acid 67 to about amino acid 83, from about amino acid 117 to about amino acid 139 and from about amino acid 153 to about amino acid 170. Clone DNA59625-1498 has been deposited with ATCC on June 16, 1998 and is assigned ATCC deposit no. 209992.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 220 (SEQ ID NO:303), evidenced significant homology between the PRO1141 amino acid sequence and the following Dayhoff sequences: CEVF36H2L_2, PCRB7PRJ_1, AB000506_1, LEU95008_1, MRU87980_15, YIGM_ECOLI, STU65700_1, GHU62778_1, CYST_SYNY3 and AF009567_1.

EXAMPLE 99: Isolation of cDNA clones Encoding Human PRO1132

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein as DNA35934. Based on the DNA35934 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1132.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'-TCCTGTGACCACCCCTCTAACACC-3' (SEQ ID NO:310) and
reverse PCR primer: 5'-CTGGAACATCTGCTGCCAGATTC-3' (SEQ ID NO:311).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus sequence which had the following nucleotide sequence:

5'-GTCGGATGACAGCAGCAGCCGCATCATCAATGGATCCGACTGCGATATGC-3' (SEQ ID NO:312).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1132 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1132 and the derived protein sequence for PRO1132.

The entire nucleotide sequence of PRO1132 is shown in Figure 225 (SEQ ID NO:308). Clone DNA59767-1489 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 354-356 and a stop codon at nucleotide positions 1233-1235 (Figure 225; SEQ ID NO:308). The predicted polypeptide precursor is 293 amino acids long. The signal peptide is at about amino acids 1-22 and the histidine active site is at about amino acids 104-109 of SEQ ID NO:309. Clone DNA59767-1489 has been deposited with ATCC (having the actual sequence rather than representations based on sequencing techniques as presented herein) and is assigned ATCC deposit no. 203108. The full-length PRO1132 protein shown in Figure 226 has an estimated molecular weight of about 32,020 daltons and a pI of about 8.7.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 226 (SEQ ID NO:309), revealed sequence identity between the PRO1132 amino acid sequence and the following Dayhoff sequences: SSU76256_1, P_W10694, MMAE000663_6, AF013988_1, U66061_8, MMAE000665_2, MMAE00066415, MMAE00066414, MMAE000665_4 and MMAE00066412.

EXAMPLE 100: Isolation of cDNA clones Encoding Human NL7 (PRO1346)

A single EST sequence (#1398422) was found in the LIFESEQ[®] database as described in Example 1 above. This EST sequence was renamed as DNA45668. Based on the DNA45668 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for NL7.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'-CACACGTCCAACCTCAATGGGCAG-3' (SEQ ID NO:315)

reverse PCR primer: 5'-GACCAGCAGGGCCAAGGACAAGG-3' (SEQ ID NO:316)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA45668 sequence which had the following nucleotide sequence:

hybridization probe:

5'-GTTCTCTGAGATGAAGATCCGGCCGGTCCGGGAGTACCGCTTAG-3'

(SEQ ID NO:317)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the NL7 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from a human fetal kidney library (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for NL7 (designated herein as DNA59776-1600 [Figure 227, SEQ ID NO:313]) and the derived protein sequence for NL7 (PRO1346).

The entire coding sequence of NL7 (PRO1346) is shown in Figure 227 (SEQ ID NO:313). Clone DNA59776-1600 contains a single open reading frame with an apparent translational initiation site at nucleotide

positions 1-3 and an apparent stop codon at nucleotide positions 1384-1386. The predicted polypeptide precursor is 461 amino acids long. The protein contains an apparent type II transmembrane domain at amino acid positions from about 31 to about 50; fibrinogen beta and gamma chains C-terminal domain signature starting at about amino acid position 409, and a leucine zipper pattern starting at about amino acid positions 140, 147, 154 and 161, respectively. Clone DNA59776-1600 has been deposited with ATCC and is assigned ATCC deposit no. 203128. The full-length NL7 protein shown in Figure 228 has an estimated molecular weight of about 50,744 daltons and a pI of about 6.38.

Based on a WU-BLAST2 sequence alignment analysis (using the WU-BLAST2 computer program) of the full-length sequence, NL7 shows significant amino acid sequence identity to a human microfibril-associated glycoprotein (1 MFA4_HUMAN); to known TIE-2 ligands and ligand homologues, ficolin, serum lectin and TGF-1 binding protein.

EXAMPLE 101: Isolation of cDNA clones Encoding Human PRO1131

A cDNA sequence isolated in the amylase screen described in Example 2 above is herein designated DNA43546 (see Figure 231; SEQ ID NO:320). The DNA43546 sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA45627.

Based on the DNA45627 sequence, oligonucleotide probes were generated and used to screen a human library prepared as described in paragraph 1 of Example 2 above. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

PCR primers (forward and 2 reverse) were synthesized:

forward PCR primer 5'-ATGCAGGCCAAGTACAGCAGCAC-3' (SEQ ID NO:321);

reverse PCR primer 1 5'-CATGCTGACGACTTCCTGCAAGC-3' (SEQ ID NO:322); and

reverse PCR primer 1 5'-CCACACAGTCTCTGCTTCTTGGG-3' (SEQ ID NO:323)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA45627 sequence which had the following nucleotide sequence:

hybridization probe

5'-ATGCTGGATGATGATGGGGACACCACCATGAGCCTGCATT-3' (SEQ ID NO:324).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1131 gene using the probe oligonucleotide and one of the PCR primers.

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 144-146, and a stop signal at nucleotide positions 984-986 (Figure 229; SEQ ID NO:318). The predicted polypeptide precursor is 280 amino acids long, has a calculated molecular weight of approximately 31,966 daltons and an estimated pI of approximately 6.26. The transmembrane domain sequence is at about 49-74 of SEQ ID NO:319 and the region having sequence identity with LDL receptors is about 50-265 of SEQ ID NO:319. PRO1131 contains potential N-linked glycosylation sites at amino acid positions 95-98 and 169-172 of SEQ ID NO:319. Clone DNA59777-1480 has been deposited with the ATCC and is assigned ATCC deposit no. 203111.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 230 (SEQ ID NO:319), evidenced some sequence identity between the PRO1131 amino acid sequence and the following Dayhoff sequences: AB010710_1, I49053, I49115, RNU56863_1, LY4A_MOUSE, I55686, MMU56404_1, I49361, AF030313_1 and MMU09739_1.

EXAMPLE 102: Isolation of cDNA clones Encoding Human PRO1281

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein as DNA35720. Based on the DNA35720 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1281.

PCR primers (forward and reverse) were synthesized:

forward PCR primers:

- 20 5'-TGGAAGGCTGCCGCAACGACAATC-3' (SEQ ID NO:327);
5'-CTGATGTGGCCGATGTTCTG-3' (SEQ ID NO:328); and
5'-ATGGCTCAGTGTGCAGACAG-3' (SEQ ID NO:329).

reverse PCR primers:

- 5'-GCATGCTGCTCCGTGAAGTAGTCC-3' (SEQ ID NO:330); and
25 5'-ATGCATGGGAAAGAAGGCCTGCCC-3' (SEQ ID NO:331).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA35720 sequence which had the following nucleotide sequence:

hybridization probe:

- 5'-TGCACTGGTGACCACGAGGGGGTGCATATAGCCATCTGGAGCTGAG-3' (SEQ ID NO:332).
30 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO1281 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1281 (designated herein as DNA59820-1549 [Figure 232, SEQ ID NO:325]; and the derived protein sequence for PRO1281.

The entire coding sequence of PRO1281 is shown in Figure 232 (SEQ ID NO:325). Clone DNA59820-1549 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 228-230 and an apparent stop codon at nucleotide positions 2553-2555. The predicted polypeptide precursor is 775 amino acids long. The full-length PRO1281 protein shown in Figure 233 has an estimated molecular weight of about 85,481 daltons and a pI of about 6.92. Additional features include a signal peptide at about amino acids 1-15; and potential N-glycosylation sites at about amino acids 138-141 and 361-364.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 233 (SEQ ID NO:326), revealed some sequence identity between the PRO1281 amino acid sequence and the following Dayhoff sequences: S44860, CET24D1_1, CEC38H2_3, CAC2_HAECO, B3A2_HUMAN, S22373, CEF38A3_2, CEC34F6_2, CEC34F6_3, and CELT22B11_3.

Clone DNA59820-1549 has been deposited with ATCC and is assigned ATCC deposit no. 203129.

EXAMPLE 103: Isolation of cDNA clones Encoding Human PRO1064

A cDNA sequence isolated in the amylase screen described in Example 2 above was found, by the WU-BLAST2 sequence alignment computer program, to have no significant sequence identity to any known human protein. This cDNA sequence is herein designated DNA45288. The DNA45288 sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ[®], Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence is herein designated DNA48609. Oligonucleotide primers based upon the DNA48609 sequence were then synthesized and employed to screen a human fetal kidney cDNA library which resulted in the identification of the DNA59827-1426 clone shown in Figure 234. The cloning vector was pRK5B (pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)), and the cDNA size cut was less than 2800 bp.

The oligonucleotide probes employed were as follows:

forward PCR primer 5'-CTGAGACCCTGCAGCACCATCTG-3' (SEQ ID NO:336)

reverse PCR primer 5'-GGTGCTTCTTGAGCCCCACTTAGC-3' (SEQ ID NO:337)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA48609 sequence which had the following nucleotide sequence

hybridization probe

5'-AATCTAGCTTCTCCAGGACTGTGGTCGCCCCGTCGCTGT-3' (SEQ ID NO:338)

A full length clone was identified that contained a single open reading frame with an apparent translational initiation site at nucleotide positions 532-534 and a stop signal at nucleotide positions 991-993 (Figure 234, SEQ ID NO:333). The predicted polypeptide precursor is 153 amino acids long, has a calculated

molecular weight of approximately 17,317 daltons and an estimated pI of approximately 5.17. Analysis of the full-length PRO1064 sequence shown in Figure 235 (SEQ ID NO:334) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 24, a transmembrane domain from about amino acid 89 to about amino acid 110, an indole-3-glycerol phosphate synthase homology block from about amino acid 74 to about amino acid 105 and a Myb DNA binding domain protein repeat protein homology block from about amino acid 114 to about amino acid 137. Clone DNA59827-1426 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203089.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 235 (SEQ ID NO:334), evidenced homology between the PRO1064 amino acid sequence and the following Dayhoff sequences: MMNP15PRO_1, BP187PLYH_1, CELF42G8_4, MMU58888_1, GEN14270, TUB8_SOLTU, RCN_MOUSE, HUMRBSY79_1, SESENODA_1 and A21467_1.

EXAMPLE 104: Isolation of cDNA clones Encoding Human PRO1379

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein DNA45232. Based on the DNA45232 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1379.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-TGGACACCGTACCCTGGTATCTGC-3' (SEQ ID NO:341)
reverse PCR primer 5'-CCAACTCTGAGGAGAGCAAGTGGC-3' (SEQ ID NO:342)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA45232 sequence which had the following nucleotide sequence:

hybridization probe
 5'-TGTATGTGCACACCCTCACCATCACCTCCAAGGGCAAGGAGAAC-3' (SEQ ID NO:343).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1379 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1379 which is designated herein as DNA59828-1608 and shown in Figure 237 (SEQ ID NO:339); and the derived protein sequence for PRO1379 (SEQ ID NO:340).

The entire coding sequence of PRO1379 is shown in Figure 237 (SEQ ID NO:339). Clone DNA59828-1608 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 10-12 and an apparent stop codon at nucleotide positions 1732-1734. The predicted polypeptide precursor is 574 amino acids long. The full-length PRO1379 protein shown in Figure 238 has an estimated molecular weight of about 65,355 daltons and a pI of about 8.73. Additional features include a signal peptide at about amino acids

1-17 and potential N-glycosylation sites at about amino acids 160-163, 287-290, and 323-326.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 238 (SEQ ID NO:340), revealed some homology between the PRO1379 amino acid sequence and the following Dayhoff sequences: YHY8_YEAST, AF040625_1, HP714394_1, and HIV18U45630_1.

- 5 Clone DNA59828-1608 has been deposited with ATCC and is assigned ATCC deposit no. 203158.

EXAMPLE 105: Isolation of cDNA Clones Encoding Human PRO844

- 10 An expressed sequence tag (EST) DNA database (LIFESEQ™, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed sequence identity with aLP. Based on the information and discoveries provided herein, the clone for this EST, Incyte clone no. 2657496 from a cancerous lung library was further examined.

DNA sequencing of the insert for this clone gave a sequence (herein designated as DNA59838-1462; SEQ ID NO:344) which includes the full-length DNA sequence for PRO844 and the derived protein sequence for PRO844.

- 15 The entire nucleotide sequence of DNA59838-1462 is shown in Figure 239 (SEQ ID NO:344). Clone DNA59838-1462 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 5-7 and ending at the stop codon at nucleotide positions 338-340 of SEQ ID NO:344 (Figure 239). The predicted polypeptide precursor is 111 amino acids long (Figure 240). The full-length PRO844 protein shown in Figure 240 has an estimated molecular weight of about 12,050 daltons and a pI of about 5.45. Clone
20 UNQ544 DNA59838-1462 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

- 25 Analysis of the amino acid sequence of the full-length PRO844 polypeptide suggests that it possesses significant sequence similarity to serine protease inhibitors, thereby indicating that PRO844 may be a novel proteinase inhibitor. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO844 amino acid sequence and at least the following Dayhoff sequences, ALK1_HUMAN, P_P82403, P_P82402, ELAF_HUMAN and P_P60950.

EXAMPLE 106: Isolation of cDNA Clones Encoding Human PRO848

- 30 Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in
35 Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence

obtained therefrom is herein designated DNA55999.

In light of an observed sequence homology between the DNA55999 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2768571, the Incyte EST clone 2768571 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 241 and is herein designated as DNA59839-1461.

5 The entire nucleotide sequence of DNA59839-1461 is shown in Figure 241 (SEQ ID NO:346). Clone DNA59839-1461 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 146-148 and ending at the stop codon at nucleotide positions 1946-1948 of SEQ ID NO:346 (Figure 241). The predicted polypeptide precursor is 600 amino acids long (Figure 242). The full-length PRO848 protein shown in Figure 242 has an estimated molecular weight of about 68,536 daltons. Clone DNA59839-1461
10 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analysis of the amino acid sequence of the full-length PRO848 polypeptide suggests that it may be a novel sialyltransferase. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced sequence identity between the PRO848 amino acid sequence and at least the following Dayhoff
15 sequences, P_R78619 (GalNAc-alpha-2, 6-sialyltransferase), CAAG5_CHICK (alpha-n-acetylgalactosamide alpha-2, 6-sialyltransferase), HSU14550_1, CAG6_HUMAN and P_R63217 (human alpha-2, 3-sialyltransferase).

EXAMPLE 107: Isolation of cDNA Clones Encoding Human PRO1097

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single
20 EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90)
25 or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56006.

In light of an observed sequence homology between the DNA56006 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2408105, the Incyte EST clone 2408105 was purchased
30 and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 243 and is herein designated as DNA59841-1460.

The entire nucleotide sequence of DNA59841-1460 is shown in Figure 243 (SEQ ID NO:348). Clone DNA59841-1460 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 3-5 and ending at the stop codon at nucleotide positions 276-278 of SEQ ID NO:348 (Figure 243).
35 The predicted polypeptide precursor is 91 amino acids long (Figure 244). The full-length PRO1097 protein shown in Figure 244 has an estimated molecular weight of about 10,542 daltons and a pI of about 10.04. Clone DNA59841-1460 has been deposited with ATCC on July 1, 1998. It is understood that the deposited clone has

the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

Analyzing Figure 244, the signal peptide is at about amino acids 1-20 of SEQ ID NO:349. The glycoprotease family protein domain starts at about amino acid 56, and the acyltransferase ChoActase/COT/CPT family peptide starts at about amino acid 49 of SEQ ID NO:349.

5

EXAMPLE 108: Isolation of cDNA clones Encoding Human PRO1153

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56008.

In light of an observed sequence homology between the DNA56008 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2472409, the Incyte EST clone 2472409 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 245 and is herein designated as DNA59842-1502.

The full length clone shown in Figure 245 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 92-94 and ending at the stop codon found at nucleotide positions 683-685 (Figure 245; SEQ ID NO:350). The predicted polypeptide precursor (Figure 246, SEQ ID NO:351) is 197 amino acids long. PRO1153 has a calculated molecular weight of approximately 21,540 daltons and an estimated pI of approximately 8.31. Clone DNA59842-1502 has been deposited with ATCC and is assigned ATCC deposit no. 209982. It is understood that the correct and actual sequence is in the deposited clone while herein are present representations based on current sequencing techniques which may have minor errors.

Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1153 shows some amino acid sequence identity to the following Dayhoff designations: S57447; SOYHRGPC_1; S46965; P_P82971; VCPHEROPH_1; EXTN_TOBAC; MLCB2548_9; ANXA_RABIT; JC5437 and SSGP_VOLCA.

EXAMPLE 109: Isolation of cDNA clones Encoding Human PRO1154

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in

Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56025.

In light of an observed sequence homology between the DNA56025 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2169375, the Incyte EST clone 2169375 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 247 and is herein designated as DNA59846-1503.

The full length clone shown in Figure 247 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 86-88 and ending at the stop codon found at nucleotide positions 2909-2911 (Figure 247; SEQ ID NO:352). The predicted polypeptide precursor (Figure 248, SEQ ID NO:353) is 941 amino acids long. PRO1154 has a calculated molecular weight of approximately 107,144 daltons and an estimated pI of approximately 6.26. Clone DNA59846-1503 has been deposited with ATCC and is assigned ATCC deposit no. 209978.

Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1154 shows sequence identity to at least the following Dayhoff designations: AB011097_1, AMPN_HUMAN, RNU76997_1, 159331, GEN14047, HSU62768_1, P_R51281, CET07F10_1, SSU66371_1, and AMPRE_HUMAN.

EXAMPLE 110: Isolation of cDNA clones Encoding Human PRO1181

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database, designated herein as 82468. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56029.

In light of an observed sequence homology between the DNA56029 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2186536, the Incyte EST clone 2186536 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 249 and is herein designated as DNA59847-1511.

Clone DNA59847-1511 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 17-19 and ending at the stop codon at nucleotide positions 1328-1330 (Figure 249). The predicted polypeptide precursor is 437 amino acids long (Figure 250). The full-length PRO1181 protein shown in Figure 250 has an estimated molecular weight of about 46,363 daltons and a pI of about 6.22. Analysis of the full-length PRO1181 sequence shown in Figure 250 (SEQ ID NO:355) evidences the presence of the

following: a signal peptide from about amino acid 1 to about amino acid 15, potential N-glycosylation sites from about amino acid 46 to about amino acid 49, from about amino acid 189 to about amino acid 192 and from about amino acid 382 to about amino acid 385 and amino acid sequence blocks having homology to Ly-6/u-PAR domain proteins from about amino acid 287 to about amino acid 300 and from about amino acid 98 to about amino acid 111. Clone DNA59847-1511 has been deposited with ATCC on August 4, 1998 and is assigned
 5 ATCC deposit no. 203098.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 250 (SEQ ID NO:355), evidenced homology between the PRO1181 amino acid sequence and the following Dayhoff sequences: AF041083_1, P_W26579, RNMAPIAN_1, CELT13C2_2, LMSAP2GN_1, S61882, CEF35C5_12, DP87_DICDI, GIU47631_1 and
 10 P_R07092.

EXAMPLE 111: Isolation of cDNA clones Encoding Human PRO1182

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database, designated herein as 146647. This EST cluster sequence was
 15 then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and
 20 assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56033.

In light of an observed sequence homology between the DNA56033 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2595195, the Incyte EST clone 2595195 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.
 25 The sequence of this cDNA insert is shown in Figure 251 and is herein designated as DNA59848-1512.

Clone DNA59848-1512 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 67-69 and ending at the stop codon at nucleotide positions 880-882 (Figure 251). The predicted polypeptide precursor is 271 amino acids long (Figure 252). The full-length PRO1182 protein shown in Figure 252 has an estimated molecular weight of about 28,665 daltons and a pI of about 5.33. Analysis of
 30 the full-length PRO1182 sequence shown in Figure 252 (SEQ ID NO:357) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25, an amino acid block having homology to C-type lectin domain proteins from about amino acid 247 to about amino acid 256 and an amino acid sequence block having homology to C1q domain proteins from about amino acid 44 to about amino acid 77. Clone DNA59848-1512 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit
 35 no. 203088.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 252 (SEQ ID NO:357), evidenced significant

homology between the PRO1182 amino acid sequence and the following Dayhoff sequences: PSPD_BOVIN, CL43_BOVIN, CONG_BOVIN, P_W18780, P_R45005, P_R53257 and CELEGAP7_1.

EXAMPLE 112: Isolation of cDNA clones Encoding Human PRO1155

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single
 5 EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of
 expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary
 EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The
 homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in
Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90)
 10 or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with
 the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence
 obtained therefrom is herein designated DNA56102.

In light of an observed sequence homology between the DNA56102 consensus sequence and an EST
 sequence encompassed within the Incyte EST clone no. 2858870, the Incyte EST clone 2858870 was purchased
 15 and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.
 The sequence of this cDNA insert is shown in Figure 253 and is herein designated as DNA59849-1504.

The full length clone shown in Figure 253 contained a single open reading frame with an apparent
 translational initiation site at nucleotide positions 158-160 and ending at the stop codon found at nucleotide
 positions 563-565 (Figure 253; SEQ ID NO:358). The predicted polypeptide precursor (Figure 254, SEQ ID
 20 NO:359) is 135 amino acids long. PRO1155 has a calculated molecular weight of approximately 14,833 daltons
 and an estimated pI of approximately 9.78. Clone DNA59849-1504 has been deposited with ATCC and is
 assigned ATCC deposit no. 209986. It is understood that the actual clone has the correct sequence whereas
 herein are only representations which are prone to minor sequencing errors.

Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-
 25 length sequence, PRO1155 shows some amino acid sequence identity with the following Dayhoff designations:
 TKNK_BOVIN; PVB19X587_1; AF019049_1; P_W00948; S72864; P_W00949; I62742; AF038501_1;
 TKNG_HUMAN; and YAT1_RHOBL. Based on the information provided herein, PRO1155 may play a role
 in providing neuroprotection and cognitive enhancement.

EXAMPLE 113: Isolation of cDNA clones Encoding Human PRO1156

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single
 EST cluster sequence from the Incyte database, designated herein as 138851. This EST cluster sequence was
 then compared to a variety of expressed sequence tag (EST) databases which included public EST databases
 (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to
 35 identify existing homologies. The homology search was performed using the computer program BLAST or
 BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a
 BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and

assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56261.

In light of an observed sequence homology between the DNA56261 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3675191, the Incyte EST clone 3675191 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.

- 5 The sequence of this cDNA insert is shown in Figure 255 and is herein designated as DNA59853-1505.

The full length clone shown in Figure 255 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 212-214 and ending at the stop codon found at nucleotide positions 689-691 (Figure 255; SEQ ID NO:360). The predicted polypeptide precursor (Figure 256, SEQ ID NO:361) is 159 amino acids long. PRO1156 has a calculated molecular weight of approximately 17,476 daltons, 10 an estimated pI of approximately 9.15, a signal peptide sequence at about amino acids 1 to about 22, and potential N-glycosylation sites at about amino acids 27-30 and 41-44.

Clone DNA59853-1505 was deposited with the ATCC on June 16, 1998 and is assigned ATCC deposit no. 209985.

- 15 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence shown in Figure 256 (SEQ ID NO:361), revealed some homology between the PRO1156 amino acid sequence and the following Dayhoff sequences: D45027_1, P_R79914, JC5309, KBF2_HUMAN, AF010144_1, GEN14351, S68681, P_R79915, ZMTAC_3, and HUMCPGO_1.

20 EXAMPLE 114: Isolation of cDNA Clones Encoding Human PRO1098

- Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ[®], Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The 25 homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56377.

- 30 In light of an observed sequence homology between the DNA56377 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3050917, the Incyte EST clone 3050917 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 257 and is herein designated as DNA59854-1459.

- The entire nucleotide sequence of DNA59854-1459 is shown in Figure 257 (SEQ ID NO:362). Clone 35 DNA59854-1459 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 58-60 and ending at the stop codon at nucleotide positions 292-294 of SEQ ID NO:362 (Figure 257). The predicted polypeptide precursor is 78 amino acids long (Figure 258). The full-length PRO1098 protein

shown in Figure 258 has an estimated molecular weight of about 8,396 daltons and a pI of about 7.66. Clone DNA59854-1459 has been deposited with ATCC on June 16, 1998. It is understood that the deposited clone has the actual nucleic acid sequence and that the sequences provided herein are based on known sequencing techniques.

- 5 Analyzing Figure 258, a signal peptide appears to be at about amino acids 1-19 of SEQ ID NO:363, an N-glycosylation site appears to be at about amino acids 37-40 of SEQ ID NO:363, and N-myristoylation sites appear to be at about 15-20, 19-24 and 60-65 of SEQ ID NO:363.

EXAMPLE 115: Isolation of cDNA clones Encoding Human PRO1127

- Use of the signal sequence algorithm described in Example 3 above allowed identification of a single
10 EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90)
15 or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57959.

- In light of an observed sequence homology between the DNA57959 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 685126, the Merck EST clone 685126 was purchased
20 and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 259 and is herein designated as DNA60283-1484.

- The full length clone shown in Figure 259 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 126-128 and ending at the stop codon found at nucleotide positions 327-329 (Figure 259; SEQ ID NO:364). The predicted polypeptide precursor (Figure 260, SEQ ID
25 NO:365) is 67 amino acids long including a signal peptide at about 1-29 of SEQ ID NO:365. PRO1127 has a calculated molecular weight of approximately 7,528 daltons and an estimated pI of approximately 4.95. Clone DNA60283-1484 was deposited with the ATCC on July 1, 1998 and is assigned ATCC deposit no. 203043. It is understood that the deposited clone has the actual sequence, whereas representations which may have minor sequencing errors are presented herein.

- 30 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 260 (SEQ ID NO:365), revealed some homology between the PRO1127 amino acid sequence and the following Dayhoff sequences: AF037218_48, P_W09638, HBA_HETPO, S39821, KR2_EBV, CET20D3_8, HCU37630_1, HS193B12_10, S40012 and TRITUBC_1.

35

EXAMPLE 116: Isolation of cDNA clones Encoding Human PRO1126

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56250.

- 10 In light of an observed sequence homology between the DNA56250 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1437250, the Incyte EST clone 1437250 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 261 and is herein designated as DNA60615-1483.

- 15 Clone DNA60615-1483 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 110-112 and ending at the stop codon at nucleotide positions 1316-1318 (Figure 261). The predicted polypeptide precursor is 402 amino acids long (Figure 262). The full-length PRO1126 protein shown in Figure 262 has an estimated molecular weight of about 45,921 daltons and a pI of about 8.60. Analysis of the full-length PRO1126 sequence shown in Figure 262 (SEQ ID NO:367) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 25 and potential N-glycosylation sites from about amino acid 66 to about amino acid 69, from about amino acid 138 to about amino acid 141 and from about amino acid 183 to about amino acid 186. Clone DNA60615-1483 has been deposited with ATCC on June 16, 1998 and is assigned ATCC deposit no. 209980.

- 20 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 262 (SEQ ID NO:367), evidenced significant homology between the PRO1126 amino acid sequence and the following Dayhoff sequences: I73636, NOMR_HUMAN, MMUSMYOC3_1, HS454G6_1, P_R98225, RNU78105_1, RNU72487_1, AF035301_1, CEELC48E7_4 and CEF11C3_3.

EXAMPLE 117: Isolation of cDNA clones Encoding Human PRO1125

- 30 Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence

obtained therefrom is herein designated DNA56540.

In light of an observed sequence homology between the DNA56540 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1486114, the Incyte EST clone 1486114 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 263 and is herein designated as DNA60615-1483.

- 5 The full length clone shown in Figure 263 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 47-49 and ending at the stop codon found at nucleotide positions 1388-1390 (Figure 263; SEQ ID NO:368). The predicted polypeptide precursor (Figure 264, SEQ ID NO:369) is 447 amino acids long. PRO1125 has a calculated molecular weight of approximately 49,798 daltons and an estimated pI of approximately 9.78. Clone DNA60619-1482 has been deposited with ATCC and is assigned
10 ATCC deposit no. 209993. It is understood that the clone has the actual sequence and that the sequences herein are representations based on current techniques which may be prone to minor errors.

- Based on a WU-BLAST2 sequence alignment analysis (using the ALIGN computer program) of the full-length sequence, PRO1125 shows some sequence identity with the following Dayhoff designations: RCO1_NEUCR; S58306; PKWA_THECU; S76086; P_R85881; HET1_PODAN; SPU92792_1;
15 APAF_HUMAN; S76414 and S59317.

EXAMPLE 118: Isolation of cDNA clones Encoding Human PRO1186

- Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of
20 expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with
25 the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56748.

- In light of an observed sequence homology between the DNA56748 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3476792, the Incyte EST clone 3476792 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.
30 The sequence of this cDNA insert is shown in Figure 265 and is herein designated as DNA60621-1516.

- The full length clone shown in Figure 265 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 91-93 and ending at the stop codon found at nucleotide positions 406-408 (Figure 265; SEQ ID NO:370). The predicted polypeptide precursor (Figure 266, SEQ ID NO:371) is 105 amino acids long. The signal peptide is at amino acids 1-19 of SEQ ID NO:371. PRO1186 has a
35 calculated molecular weight of approximately 11,715 daltons and an estimated pI of approximately 9.05. Clone DNA60621-1516 was deposited with the ATCC on August 4, 1998 and is assigned ATCC deposit no. 203091.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 266 (SEQ ID NO:371), revealed some sequence identity between the PRO1186 amino acid sequence and the following Dayhoff sequences: VPRA_DENPO, LFE4_CHICK, AF034208_1, AF030433_1, A55035, COL_RABIT, CELB0507_9, S67826_1, S34665 and CRU73817_1.

5

EXAMPLE 119: Isolation of cDNA clones Encoding Human PRO1198

An initial DNA sequence referred to herein as DNA52083 was identified using a yeast screen in a human umbilical vein endothelial cell cDNA library that preferentially represents the 5' ends of the primary cDNA clones. DNA52083 was compared to ESTs from public databases (e.g., GenBank), and a proprietary
10 EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA), using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. The ESTs were clustered and assembled into a consensus DNA sequence using the computer program "phrap" (Phil Green, University of Washington, Seattle, Washington). One or more of the ESTs was obtained from human breast skin tissue biopsy. This consensus sequence is designated herein as DNA52780.

15 In light of an observed sequence homology between the DNA52780 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3852910, the Incyte EST clone 3852910 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 267 and is herein designated as DNA60622-1525.

The full length DNA60622-1525 clone shown in Figure 267 (SEQ ID NO:372) contained a single open
20 reading frame with an apparent translational initiation site at nucleotide positions 54 to 56 and ending at the stop codon found at nucleotide positions 741 to 743. The predicted polypeptide precursor, which is shown in Figure 268 (SEQ ID NO:373), is 229 amino acids long. PRO1198 has a calculated molecular weight of approximately 25,764 daltons and an estimated pI of approximately 9.17. There is a signal peptide sequence at about amino acids 1 through 34. There is sequence identity with glycosyl hydrolases family 31 protein at about amino acids
25 142 to about 175.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 268 (SEQ ID NO:373), revealed some homology between the PRO1198 amino acid sequence and the following Dayhoff sequences: ATF6H11_6, UCRI_RAT, TOBSUP2NT_1, RCUERF3_1, AMU88186_1, P_W22485, S56579, AF040711_1, DPP4_PIG.

30 Clone DNA60622-1525 was been deposited with the ATCC on August 4, 1998, and is assigned ATCC deposit no. 203090.

EXAMPLE 120: Isolation of cDNA clones Encoding Human PRO1158

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single
35 EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The

homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57248.

- 5 In light of an observed sequence homology between the DNA57248 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2640776, the Incyte EST clone 2640776 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 269 and is herein designated as DNA60625-1507.

- 10 The full length clone shown in Figure 269 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 163 to 165 and ending at the stop codon found at nucleotide positions 532 to 534 (Figure 269; SEQ ID NO:374). The predicted polypeptide precursor (Figure 270, SEQ ID NO:375) is 123 amino acids long. PRO1158 has a calculated molecular weight of approximately 13,113 daltons and an estimated pI of approximately 8.53. Additional features include a signal peptide sequence at about amino acids 1-19, a transmembrane domain at about amino acids 56-80, and a potential N-glycosylation site at
15 about amino acids 36-39. Clone DNA60625-1507 was deposited with the ATCC on June 16, 1998 and is assigned ATCC deposit no. 209975.

- An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 270 (SEQ ID NO:375), revealed some homology between the PRO1158 amino acid sequence and the following Dayhoff sequences: ATAC00310510F18A8.10,
20 P_R85151, PHS2_SOLTU, RNMHCIBAC_1, RNA1FMHC_1, I68771, RNRT1A10G_1, PTPA_HUMAN, HUMGACA_1, and CHKPTPA_1.

EXAMPLE 121: Isolation of cDNA clones Encoding Human PRO1159

- Use of the signal sequence algorithm described in Example 3 above allowed identification of a single
25 EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90)
30 or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57221.

- In light of an observed sequence homology between the DNA57221 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 376776, the Incyte EST clone 376776 was purchased
35 and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 271 and is herein designated as DNA60627-1508.

Clone DNA60627-1508 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 92-94 and ending at the stop codon at nucleotide positions 362-364 (Figure 271). The predicted polypeptide precursor is 90 amino acids long (Figure 272). The full-length PRO1159 protein shown in Figure 272 has an estimated molecular weight of about 9,840 daltons and a pI of about 10.13. Analysis of the full-length PRO1159 sequence shown in Figure 272 (SEQ ID NO:377) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 15 and a potential N-glycosylation site from about amino acid 38 to about amino acid 41. Clone DNA60627-1508 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203092.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 272 (SEQ ID NO:377), evidenced significant homology between the PRO1159 amino acid sequence and the following Dayhoff sequences: AF016494_6, AF036708_20, DSSCUTE_1, D89100_1, S28060, MEFA_XENLA, AF020798_12, G70065, E64423, JQ2005.

EXAMPLE 122: Isolation of cDNA clones Encoding Human PRO1124

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ[®], Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56035.

In light of an observed sequence homology between the DNA56035 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 2767646, the Incyte EST clone 2767646 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 273 and is herein designated as DNA60629-1481.

The full length clone shown in Figure 273 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 25-27 and ending at the stop codon found at nucleotide positions 2782-2784 (Figure 273; SEQ ID NO:378). The predicted polypeptide precursor (Figure 274, SEQ ID NO:379) is 919 amino acids long. PRO1124 has a calculated molecular weight of approximately 101,282 daltons and an estimated pI of approximately 5.37. Clone DNA60629-1481 has been deposited with the ATCC and is assigned ATCC deposit no. 209979. It is understood that the deposited clone has the actual sequence, whereas only representations based on current sequencing techniques which may include normal and minor errors, are provided herein.

Based on a WU-BLAST2 sequence alignment analysis of the full-length sequence, PRO1124 shows significant amino acid sequence identity to a chloride channel protein and to ECAM-1. Specifically, the following Dayhoff designations were identified as having sequence identity with PRO1124: ECLC_BOVIN,

AF001261_1, P_W06548, SSC6A10_1, AF004355_1, S76691, AF017642, BYU06866_2, CSA_DICDI and SAU47139_2.

EXAMPLE 123: Isolation of cDNA clones Encoding Human PRO1287

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed homology to the fringe protein. This EST sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence obtained is herein designated DNA40568.

Based on the DNA40568 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1287. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, *supra*, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTCGGGGAAAGGGACTTGATGTTGG-3' (SEQ ID NO:382)

reverse PCR primer 1 5'-GCGAAGGTGAGCCTCTATCTCGTGCC-3' (SEQ ID NO:383)

25 reverse PCR primer 2 5'-CAGCCTACACGTATTGAGG-3' (SEQ ID NO:384)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40568 sequence which had the following nucleotide sequence

hybridization probe

5'-CAGTCAGTACAATCCTGGCATAATATACGGCCACCATGATGCAGTCCC-3' (SEQ ID NO:385).

30 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO1287 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human bone marrow tissue. The cDNA libraries used to isolated the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to SalI hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD;

pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1287 (designated herein as DNA61755-1554 [Figure 275, SEQ ID NO:380]) and the derived protein sequence for PRO1287.

- 5 The entire nucleotide sequence of DNA61755-1554 is shown in Figure 275 (SEQ ID NO:380). The full length clone contained a single open reading frame with an apparent translational initiation site at nucleotide positions 655-657 and a stop signal at nucleotide positions 2251-2253 (Figure 275, SEQ ID NO:380). The predicted polypeptide precursor is 532 amino acids long, has a calculated molecular weight of approximately 61,351 daltons and an estimated pI of approximately 8.77. Analysis of the full-length PRO1287 sequence shown
10 in Figure 276 (SEQ ID NO:381) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 27 and potential N-glycosylation sites from about amino acid 315 to about amino acid 318 and from about amino acid 324 to about amino acid 327. Clone DNA61755-1554 has been deposited with ATCC on August 11, 1998 and is assigned ATCC deposit no. 203112.

- An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence
15 alignment analysis of the full-length sequence shown in Figure 276 (SEQ ID NO:381), evidenced significant homology between the PRO1287 amino acid sequence and the following Dayhoff sequences: CET24D1_1, EZRI_BOVIN, GGU19889_1, CC3_YEAST, S74244, NALS_MOUSE, MOES_PIG, S28660, S44860 and YNA4_CAEEL.

20 EXAMPLE 124: Isolation of cDNA clones Encoding Human PRO1312

DNA55773 was identified in a human fetal kidney cDNA library using a yeast screen that preferentially represents the 5' ends of the primary cDNA clones. Based on the DNA55773 sequence, oligonucleotides were synthesized for use as probes to isolate a clone of the full-length coding sequence for PRO1312.

- The full length DNA61873-1574 clone shown in Figure 277 (SEQ ID NO:386) contained a single open
25 reading frame with an apparent translational initiation site at nucleotide positions 7-9 and ending at the stop codon found at nucleotide positions 643-645. The predicted polypeptide precursor is 212 amino acids long (Figure 278, SEQ ID NO:387). PRO1312 has a calculated molecular weight of approximately 24,024 daltons and an estimated pI of approximately 6.26. Other features include a signal peptide at about amino acids 1-14; a transmembrane domain at about amino acids 141-160, and potential N-glycosylation sites at about amino acids
30 76-79 and 93-96.

- An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence
alignment analysis of the full-length sequence shown in Figure 278 (SEQ ID NO:387), revealed some homology between the PRO1312 amino acid sequence and the following Dayhoff sequences: GCINTALPH_1, GIBMUC1A_1, P_R96298, AF001406_1, PVU88874_1, P_R85151, AF041409_1, CELC50F2_7, C45875,
35 and AB009510_21.

Clone DNA61873-1574 has been deposited with ATCC and is assigned ATCC deposit no. 203132.

EXAMPLE 125: Isolation of cDNA clones Encoding Human PRO1192

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein DNA35924. Based on the DNA35924 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1192.

PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'-CCGAGGCCATCTAGAGGCCAGAGC-3' (SEQ ID NO:390)

reverse PCR primer: 5'-ACAGGCAGAGCCAATGGCCAGAGC-3' (SEQ ID NO:391).

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35924 sequence which had the following nucleotide sequence:

hybridization probe:

5'-GAGAGGACTGCGGGAGTTTGGGACCTTTGTGCAGACGTGCTCATG-3' (SEQ ID NO:392).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1192 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver and spleen tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1192 designated herein as DNA62814-1521 and shown in Figure 279 (SEQ ID NO:388); and the derived protein sequence for PRO1192 which is shown in Figure 280 (SEQ ID NO:389).

The entire coding sequence of PRO1192 is shown in Figure 279 (SEQ ID NO:388). Clone DNA62814-1521 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and an apparent stop codon at nucleotide positions 766-768. The predicted polypeptide precursor is 215 amino acids long. The predicted polypeptide precursor has the following features: a signal peptide at about amino acids 1-21; a transmembrane domain at about amino acids 153-176; potential N-glycosylation sites at about amino acids 39-42 and 118-121; and homology with myelin P0 proteins at about amino acids 27-68 and 99-128 of Figure 280. The full-length PRO1192 protein shown in Figure 280 has an estimated molecular weight of about 24,484 daltons and a pI of about 6.98.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 280 (SEQ ID NO:389), revealed homology between the PRO1192 amino acid sequence and the following Dayhoff sequences: GEN12838, MYPO_HUMAN, AF049498_1, GEN14531, P_W14146, HS46KDA_1, CINB_RAT, OX2G_RAT, D87018_1, and D86996_2.

Clone DNA62814-1521 was deposited with the ATCC on August 4, 1998, and is assigned ATCC deposit no. 203093.

EXAMPLE 126: Isolation of cDNA clones Encoding Human PRO1160

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA40650. Based on the DNA40650 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1160.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-GCTCCCTGATCTTCATGTCACCACC-3' (SEQ ID NO:395)

reverse PCR primer 5'-CAGGGACACACTCTACCATTCGGGAG-3' (SEQ ID NO:396)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40650 sequence which had the following nucleotide sequence

hybridization probe

5'-CCATCTTTCTGGTCTCTGCCCAGAATCCGACAACAGCTGCTC-3' (SEQ ID NO:397)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1160 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1160 (designated herein as DNA62872-1509 [Figure 281, SEQ ID NO: 393]) and the derived protein sequence for PRO1160.

The entire nucleotide sequence of DNA62872-1509 is shown in Figure 281 (SEQ ID NO:393). Clone DNA62872-1509 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 40-42 and ending at the stop codon at nucleotide positions 310-312 (Figure 281). The predicted polypeptide precursor is 90 amino acids long (Figure 282). The full-length PRO1160 protein shown in Figure 282 has an estimated molecular weight of about 9,039 daltons and a pI of about 4.37. Analysis of the full-length PRO1160 sequence shown in Figure 282 (SEQ ID NO:394) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19 and a protein kinase C phosphorylation site from about amino acid 68 to about amino acid 70. Clone DNA62872-1509 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203100.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 282 (SEQ ID NO:394), evidenced significant homology between the PRO1160 amino acid sequence and the following Dayhoff sequences: B30305, GEN13490, I53641, S53363, HA34_BRELC, SP96_DICDI, S36326, SSU51197_10, MUC1_XENLA, TCU32448_1 and AF000409_1.

EXAMPLE 127: Isolation of cDNA clones Encoding Human PRO1187

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of

expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57726.

In light of an observed sequence homology between the DNA57726 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 358563, the Incyte EST clone 358563 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 283 and is herein designated as DNA62876-1517.

The full length clone shown in Figure 283 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and ending at the stop codon found at nucleotide positions 481-483 (Figure 283; SEQ ID NO:398). The predicted polypeptide precursor (Figure 284, SEQ ID NO:399) is 120 amino acids long. The signal peptide is at about amino acids 1-17 of SEQ ID NO:399. PRO1187 has a calculated molecular weight of approximately 12,925 daltons and an estimated pI of approximately 9.46. Clone DNA62876-1517 was deposited with the ATCC on August 4, 1998 and is assigned ATCC deposit no. 203095. It is understood that the deposited clone contains the actual sequence and that the representations herein may have minor sequencing errors.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 284 (SEQ ID NO:399), revealed some sequence identity (and therefore some relation) between the PRO1187 amino acid sequence and the following Dayhoff sequences: MGNENDOBX_1, CELF41G3_9, AMPG_STRLI, HSBBOVHERL_2, LEEXTEN10_1, AF029958_1 and P_W04957.

EXAMPLE 128: Isolation of cDNA clones Encoding Human PRO1185

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56426.

In light of an observed sequence homology between the DNA56426 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3284411, the Incyte EST clone 3284411 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein.

The sequence of this cDNA insert is shown in Figure 285 and is herein designated as DNA62881-1515.

The full length DNA62881-1515 clone shown in Figure 285 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 4-6 and ending at the stop codon found at nucleotide positions 598-600 (Figure 285; SEQ ID NO:400). The predicted polypeptide precursor (Figure 286, SEQ ID NO:401) is 198 amino acids long. The signal peptide is at about amino acids 1-21 of SEQ ID NO:401.

5 PRO1185 has a calculated molecular weight of approximately 22,105 daltons and an estimated pI of approximately 7.73. Clone DNA62881-1515 has been deposited with the ATCC and is assigned ATCC deposit no. 203096.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 286 (SEQ ID NO:401), revealed some sequence identity between the PRO1185 amino acid sequence and the following Dayhoff sequences: TUP1_YEAST, AF041382_1, MAOM_SOLTU, SPPBPHU9_1, I41024, EPCPLCFAIL_1, HSPLEC_1, YKL4_CAEEL, A44643, TGU65922_1.

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EXAMPLE 129: Isolation of cDNA clones Encoding Human PRO1345

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA47364. Based on the DNA47364 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1345.

20 PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CCTGGTTATCCCCAGGAAGTCCGAC-3' (SEQ ID NO:404)

reverse PCR primer 5'-CTCTTGCTGCTGCGACAGGCCTC-3' (SEQ ID NO:405)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47364 sequence which had the following nucleotide sequence

25 hybridization probe

5'-CGCCCTCCAAGACTATGGTAAAAGGAGCCTGCCAGGTGTCAATGAC-3' (SEQ ID NO:406)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1345 gene using the probe oligonucleotide and one of the PCR primers. RNA

30 for construction of the cDNA libraries was isolated from human breast carcinoma tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1345 (designated herein as DNA64852-1589 [Figure 287, SEQ ID NO:402]) and the derived protein sequence for PRO1345.

The entire nucleotide sequence of DNA64852-1589 is shown in Figure 287 (SEQ ID NO:402). Clone

35 DNA64852-1589 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 7-9 or 34-36 and ending at the stop codon at nucleotide positions 625-627 (Figure 287). The predicted polypeptide precursor is 206 amino acids long (Figure 288). The full-length PRO1345 protein shown in Figure

288 has an estimated molecular weight of about 23,190 daltons and a pI of about 9.40. Analysis of the full-length PRO1345 sequence shown in Figure 288 (SEQ ID NO:403) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 31 or from about amino acid 10 to about amino acid 31 and a C-type lectin domain signature sequence from about amino acid 176 to about amino acid 190. Clone DNA64852-1589 has been deposited with ATCC on August 18, 1998 and is assigned ATCC deposit no. 203127.

- 5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 288 (SEQ ID NO:403), evidenced significant homology between the PRO1345 amino acid sequence and the following Dayhoff sequences: BTU22298_1, TETN_CARSP, TETN_HUMAN, MABA_RAT, S34198, P_W13144, MACMBPA_1, A46274, PSPD_RAT AND P_R32188.

10

EXAMPLE 130: Isolation of cDNA clones Encoding Human PRO1245

- Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary
- 15 EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence
- 20 obtained therefrom is herein designated DNA56019.

In light of an observed sequence homology between the DNA56019 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1327836, the Incyte EST clone 1327836 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 289 and is herein designated as DNA64884-1527.

- 25 The full length clone shown in Figure 289 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 79-81 and ending at the stop codon found at nucleotide positions 391-393 (Figure 289; SEQ ID NO:407). The predicted polypeptide precursor (Figure 290, SEQ ID NO:408) is 104 amino acids long, with a signal peptide sequence at about amino acid 1 to about amino acid 18. PRO1245 has a calculated molecular weight of approximately 10,100 daltons and an estimated pI of
- 30 approximately 8.76.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 290 (SEQ ID NO:408), revealed some homology between the PRO1245 amino acid sequence and the following Dayhoff sequences: SYA_THETH, GEN11167, MTV044_4, AB011151_1, RLAI2750_3, SNELIPTRA_1, S63624, C28391, A37907, and S14064.

- 35 Clone DNA64884-1245 was deposited with the ATCC on August 25, 1998 and is assigned ATCC deposit no. 203155.

EXAMPLE 131: Isolation of cDNA clones Encoding Human PRO1358

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 88718, the Incyte EST clone 88718 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 291 and is herein designated as DNA64890-1612.

The full length clone shown in Figure 291 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 86 through 88 and ending at the stop codon found at nucleotide positions 1418 through 1420 (Figure 291; SEQ ID NO:409). The predicted polypeptide precursor (Figure 292, SEQ ID NO:410) is 444 amino acids long. The signal peptide is at about amino acids 1-18 of SEQ ID NO:410. PRO1358 has a calculated molecular weight of approximately 50,719 daltons and an estimated pI of approximately 8.82. Clone DNA64890-1612 was deposited with the ATCC on August 18, 1998 and is assigned ATCC deposit no. 203131.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 292 (SEQ ID NO:410), revealed sequence identity between the PRO1358 amino acid sequence and the following Dayhoff sequences: P_W07607, AB000545_1, AB000546_1, A1AT_RAT, AB015164_1, P_P50021, COTR_CAVPO, and HAMHPP_1. The variants claimed in this application exclude these sequences.

EXAMPLE 132: Isolation of cDNA clones Encoding Human PRO1195

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55716.

In light of an observed sequence homology between the DNA55716 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3252980, the Incyte EST clone 3252980 was purchased

and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 293 and is herein designated as DNA65412-1523.

The full length clone shown in Figure 293 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 58-60 and ending at the stop codon found at nucleotide positions 511-513 (Figure 293; SEQ ID NO:411). The predicted polypeptide precursor (Figure 294, SEQ ID NO:412) is 151 amino acids long. The signal sequence is at about amino acids 1-22 of SEQ ID NO:412. PRO1195 has a calculated molecular weight of approximately 17,277 daltons and an estimated pI of approximately 5.33. Clone DNA65412-1523 was deposited with the ATCC on August 4, 1998 and is assigned ATCC deposit no. 203094.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 294 (SEQ ID NO:412), revealed some sequence identity between the PRO1195 amino acid sequence and the following Dayhoff sequences: MMU28486_1, AF044205_1, P_W31186, CELK03C7_1, F69034, EF1A_METVA, AF024540_1, SSU90353_1, MRSP_STAAU and P_R97680.

EXAMPLE 133: Isolation of cDNA clones Encoding Human PRO1270

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57951.

In light of an observed sequence homology between the DNA57951 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 124878, the Merck EST clone 124878 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 295 and is herein designated as DNA66308-1537.

Clone DNA66308-1537 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 103-105 and ending at the stop codon at nucleotide positions 1042-1044 (Figure 295). The predicted polypeptide precursor is 313 amino acids long (Figure 296). The full-length PRO1270 protein shown in Figure 296 has an estimated molecular weight of about 34,978 daltons and a pI of about 5.71. Analysis of the full-length PRO1270 sequence shown in Figure 296 (SEQ ID NO:414) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 16, a potential N-glycosylation site from about amino acid 163 to about amino acid 166 and glycosaminoglycan attachment sites from about amino acid 74 to about amino acid 77 and from about amino acid 289 to about amino acid 292. Clone DNA66308-1537 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203159.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 296 (SEQ ID NO:414), evidenced significant homology between the PRO1270 amino acid sequence and the following Dayhoff sequences: XLU86699_1, S49589, FIBA_PARPA, FIBB_HUMAN, P_R47189, AF004326_1, DRTENASCN_1, AF004327_1, P_W01411 and FIBG_BOVIN.

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EXAMPLE 134: Isolation of cDNA clones Encoding Human PRO1271

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57955.

In light of an observed sequence homology between the DNA57955 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA625350, the Merck EST clone AA625350 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 297 and is herein designated as DNA66309-1538.

Clone DNA66309-1538 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 94-96 and ending at the stop codon at nucleotide positions 718-720 (Figure 297). The predicted polypeptide precursor is 208 amino acids long (Figure 298). The full-length PRO1271 protein shown in Figure 298 has an estimated molecular weight of about 21,531 daltons and a pI of about 8.99. Analysis of the full-length PRO1271 sequence shown in Figure 298 (SEQ ID NO:416) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 31 and a transmembrane domain from about amino acid 166 to about amino acid 187. Clone DNA66309-1538 has been deposited with ATCC on September 15, 1998 and is assigned ATCC deposit no. 203235.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 298 (SEQ ID NO:416), evidenced significant homology between the PRO1271 amino acid sequence and the following Dayhoff sequences: S57180, S63257, AGA1_YEAST, BPU43599_1, YS8A_CAEEL, S67570, LSU54556_2, S70305, VGLX_HSVEB, and D88733_1.

EXAMPLE 135: Isolation of cDNA clones Encoding Human PRO1375

A Merck/Wash. U. database was searched and a Merck EST was identified. This sequence was then put in a program which aligns it with other sequences from the Swiss-Prot public database, public EST databases (e.g., GenBank, Merck/Wash. U.), and a proprietary EST database (LIFESEQ®, Incyte

Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)] as a comparison of the extracellular domain (ECD) protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

A consensus DNA sequence was assembled relative to other EST sequences using phrap. This consensus sequence is designated herein "DNA67003".

Based on the DNA67003 consensus sequence, the nucleic acid (SEQ ID NO:417) was identified in a human pancreas library. DNA sequencing of the clone gave the full-length DNA sequence for PRO1375 and the derived protein sequence for PRO1375.

The entire coding sequence of PRO1375 is shown in Figure 299 (SEQ ID NO:417). Clone DNA67004-1614 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 104-106 and an apparent stop codon at nucleotide positions 698-700 of SEQ ID NO:417. The predicted polypeptide precursor is 198 amino acids long. The transmembrane domains are at about amino acids 11-28 (type II) and 103-125 of SEQ ID NO:418. Clone DNA67004-1614 has been deposited with ATCC and is assigned ATCC deposit no. 203115. The full-length PRO1375 protein shown in Figure 300 has an estimated molecular weight of about 22,531 daltons and a pI of about 8.47.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 300 (SEQ ID NO:418), revealed sequence identity between the PRO1375 amino acid sequence and the following Dayhoff sequences: AF026198_5, CELR12C12_5, S73465, Y011_MYCPN, S64538_1, P_P8150, MUVSHPO10_1, VSH_MUMPL and CVU59751_5.

EXAMPLE 136: Isolation of cDNA clones Encoding Human PRO1385

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57952.

In light of an observed sequence homology between the DNA57952 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3129630, the Incyte EST clone 3129630 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 301 and is herein designated as DNA68869-1610.

Clone DNA68869-1610 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 26-28 and ending at the stop codon at nucleotide positions 410-412 (Figure 301). The predicted polypeptide precursor is 128 amino acids long (Figure 302). The full-length PRO1385 protein shown in Figure 302 has an estimated molecular weight of about 13,663 daltons and a pI of about 10.97. Analysis of the full-length PRO1385 sequence shown in Figure 302 (SEQ ID NO:420) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, and glycosylaminoglycan attachment sites from about amino acid 82 to about amino acid 85 and from about amino acid 91 to about amino acid 94. Clone DNA68869-1610 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203164.

- 10 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 302 (SEQ ID NO:420), evidenced low homology between the PRO1385 amino acid sequence and the following Dayhoff sequences: CELT14A8_1, LMNACHRA1_1, HXD9_HUMAN, CHKCMLF_1, HS5PP34_2, DMDRING_1, A37107_1, MMLUNGENE_1, PUM_DROME and DMU25117_1.

15 EXAMPLE 137: Isolation of cDNA clones Encoding Human PRO1387

- Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., Methods in Enzymology 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56259.

- 25 In light of an observed sequence homology between the DNA56259 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3507924, the Incyte EST clone 3507924 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 303 and is herein designated as DNA68872-1620.

- 30 Clone DNA68872-1620 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 85-87 and ending at the stop codon at nucleotide positions 1267-1269 (Figure 303). The predicted polypeptide precursor is 394 amino acids long (Figure 304). The full-length PRO1387 protein shown in Figure 304 has an estimated molecular weight of about 44,339 daltons and a pI of about 7.10. Analysis of the full-length PRO1387 sequence shown in Figure 304 (SEQ ID NO:422) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 19, a transmembrane domain from about amino acid 275 to about amino acid 296, potential N-glycosylation sites from about amino acid 76 to about amino acid 79, from about amino acid 231 to about amino acid 234, from about amino acid 302 to about amino acid 305, from about amino acid 307 to about amino acid 310 and from about amino acid 376 to about amino acid

379, and amino acid sequence blocks having homology to myelin p0 protein from about amino acid 210 to about amino acid 239 and from about amino acid 92 to about amino acid 121. Clone DNA68872-1620 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203160.

- 5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 304 (SEQ ID NO:422), evidenced significant homology between the PRO1387 amino acid sequence and the following Dayhoff sequences: P_W36955, MYP0_HETFR, HS46KDA_1, AF049498_1, MYOO_HUMAN, AF030454_1, A53268, SHPTCRA_1, P_W14146 and GEN12838.

EXAMPLE 138: Isolation of cDNA clones Encoding Human PRO1384

- 10 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA54192. Based on the DNA54192 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1384.

PCR primers (forward and reverse) were synthesized:

- 15 forward PCR primer 5'-TGCAGCCCCTGTGACACAACTGG-3' (SEQ ID NO:425)
reverse PCR primer 5'-CTGAGATAACCGAGCCATCCTCCAC-3' (SEQ ID NO:426)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA54192 sequence which had the following nucleotide sequence:

hybridization probe

- 20 5'-GGAGATAGCTGCTATGGGTTCTTCAGGCACAACCTTAACATGGGAAG-3' (SEQ ID NO:427)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1384 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver.

- 25 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1384 (designated herein as DNA71159-1617 [Figure 305, SEQ ID NO:423]; and the derived protein sequence for PRO1384.

- The entire coding sequence of PRO1384 is shown in Figure 305 (SEQ ID NO:423). Clone DNA71159-1617 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 182-184 and an apparent stop codon at nucleotide positions 869-871. The predicted polypeptide precursor is 229 amino acids long. The full-length PRO1384 protein shown in Figure 306 has an estimated molecular weight of about 26,650 daltons and a pI of about 8.76. Additional features include a type II transmembrane domain at about amino acids 32-57, and potential N-glycosylation sites at about amino acids 68-71, 120-123, and 134-137.

- 35 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 306 (SEQ ID NO:424), revealed homology between the PRO1384 amino acid sequence and the following Dayhoff sequences: AF054819_1, HSAJ1687_1, AF009511_1, AB010710_1, GEN13595, HSAJ673_1, GEN13961, AB005900_1, LECH_CHICK, AF021349_1,

and NK13_RAT.

Clone DNA71159-1617 has been deposited with ATCC and is assigned ATCC deposit no. 203135.

EXAMPLE 139: Use of PRO as a hybridization probe

5 The following method describes use of a nucleotide sequence encoding PRO as a hybridization probe. DNA comprising the coding sequence of full-length or mature PRO as disclosed herein is employed as a probe to screen for homologous DNAs (such as those encoding naturally-occurring variants of PRO) in human tissue cDNA libraries or human tissue genomic libraries.

10 Hybridization and washing of filters containing either library DNAs is performed under the following high stringency conditions. Hybridization of radiolabeled PRO-derived probe to the filters is performed in a solution of 50% formamide, 5x SSC, 0.1% SDS, 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8, 2x Denhardt's solution, and 10% dextran sulfate at 42°C for 20 hours. Washing of the filters is performed in an aqueous solution of 0.1x SSC and 0.1% SDS at 42°C.

15 DNAs having a desired sequence identity with the DNA encoding full-length native sequence PRO can then be identified using standard techniques known in the art.

EXAMPLE 140: Expression of PRO in *E. coli*

This example illustrates preparation of an unglycosylated form of PRO by recombinant expression in *E. coli*.

20 The DNA sequence encoding PRO is initially amplified using selected PCR primers. The primers should contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector. A variety of expression vectors may be employed. An example of a suitable vector is pBR322 (derived from *E. coli*; see Bolivar et al., Gene, 2:95 (1977)) which contains genes for ampicillin and tetracycline resistance. The vector is digested with restriction enzyme and dephosphorylated. The PCR amplified sequences are then ligated into the vector. The vector will preferably include sequences which encode 25 for an antibiotic resistance gene, a trp promoter, a polyhis leader (including the first six STII codons, polyhis sequence, and enterokinase cleavage site), the PRO coding region, lambda transcriptional terminator, and an argU gene.

30 The ligation mixture is then used to transform a selected *E. coli* strain using the methods described in Sambrook et al., supra. Transformants are identified by their ability to grow on LB plates and antibiotic resistant colonies are then selected. Plasmid DNA can be isolated and confirmed by restriction analysis and DNA sequencing.

Selected clones can be grown overnight in liquid culture medium such as LB broth supplemented with antibiotics. The overnight culture may subsequently be used to inoculate a larger scale culture. The cells are then grown to a desired optical density, during which the expression promoter is turned on.

35 After culturing the cells for several more hours, the cells can be harvested by centrifugation. The cell pellet obtained by the centrifugation can be solubilized using various agents known in the art, and the solubilized PRO protein can then be purified using a metal chelating column under conditions that allow tight binding of the

protein.

PRO may be expressed in *E. coli* in a poly-His tagged form, using the following procedure. The DNA encoding PRO is initially amplified using selected PCR primers. The primers will contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector, and other useful sequences providing for efficient and reliable translation initiation, rapid purification on a metal chelation column, and proteolytic removal with enterokinase. The PCR-amplified, poly-His tagged sequences are then ligated into an expression vector, which is used to transform an *E. coli* host based on strain 52 (W3110 fuhA(tonA) lon galE rpoHts(htpRts) clpP(lacIq). Transformants are first grown in LB containing 50 mg/ml carbenicillin at 30°C with shaking until an O.D.600 of 3-5 is reached. Cultures are then diluted 50-100 fold into CRAP media (prepared by mixing 3.57 g (NH₄)₂SO₄, 0.71 g sodium citrate•2H₂O, 1.07 g KCl, 5.36 g Difco yeast extract, 5.36 g Sheffield hycase SF in 500 mL water, as well as 110 mM MPOS, pH 7.3, 0.55% (w/v) glucose and 7 mM MgSO₄) and grown for approximately 20-30 hours at 30°C with shaking. Samples are removed to verify expression by SDS-PAGE analysis, and the bulk culture is centrifuged to pellet the cells. Cell pellets are frozen until purification and refolding.

E. coli paste from 0.5 to 1 L fermentations (6-10 g pellets) is resuspended in 10 volumes (w/v) in 7 M guanidine, 20 mM Tris, pH 8 buffer. Solid sodium sulfite and sodium tetrathionate is added to make final concentrations of 0.1M and 0.02 M, respectively, and the solution is stirred overnight at 4°C. This step results in a denatured protein with all cysteine residues blocked by sulfitolization. The solution is centrifuged at 40,000 rpm in a Beckman Ultracentrifuge for 30 min. The supernatant is diluted with 3-5 volumes of metal chelate column buffer (6 M guanidine, 20 mM Tris, pH 7.4) and filtered through 0.22 micron filters to clarify. The clarified extract is loaded onto a 5 ml Qiagen Ni-NTA metal chelate column equilibrated in the metal chelate column buffer. The column is washed with additional buffer containing 50 mM imidazole (Calbiochem, Utrol grade), pH 7.4. The protein is eluted with buffer containing 250 mM imidazole. Fractions containing the desired protein are pooled and stored at 4°C. Protein concentration is estimated by its absorbance at 280 nm using the calculated extinction coefficient based on its amino acid sequence.

The proteins are refolded by diluting the sample slowly into freshly prepared refolding buffer consisting of: 20 mM Tris, pH 8.6, 0.3 M NaCl, 2.5 M urea, 5 mM cysteine, 20 mM glycine and 1 mM EDTA. Refolding volumes are chosen so that the final protein concentration is between 50 to 100 micrograms/ml. The refolding solution is stirred gently at 4°C for 12-36 hours. The refolding reaction is quenched by the addition of TFA to a final concentration of 0.4% (pH of approximately 3). Before further purification of the protein, the solution is filtered through a 0.22 micron filter and acetonitrile is added to 2-10% final concentration. The refolded protein is chromatographed on a Poros R1/H reversed phase column using a mobile buffer of 0.1% TFA with elution with a gradient of acetonitrile from 10 to 80%. Aliquots of fractions with A280 absorbance are analyzed on SDS polyacrylamide gels and fractions containing homogeneous refolded protein are pooled. Generally, the properly refolded species of most proteins are eluted at the lowest concentrations of acetonitrile since those species are the most compact with their hydrophobic interiors shielded from interaction with the reversed phase resin. Aggregated species are usually eluted at higher acetonitrile concentrations. In addition to resolving misfolded forms of proteins from the desired form, the reversed phase step also removes endotoxin

from the samples.

Fractions containing the desired folded PRO polypeptide are pooled and the acetonitrile removed using a gentle stream of nitrogen directed at the solution. Proteins are formulated into 20 mM Hepes, pH 6.8 with 0.14 M sodium chloride and 4% mannitol by dialysis or by gel filtration using G25 Superfine (Pharmacia) resins equilibrated in the formulation buffer and sterile filtered.

- 5 Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 141: Expression of PRO in mammalian cells

This example illustrates preparation of a potentially glycosylated form of PRO by recombinant expression in mammalian cells.

- 10 The vector, pRK5 (see EP 307,247, published March 15, 1989), is employed as the expression vector. Optionally, the PRO DNA is ligated into pRK5 with selected restriction enzymes to allow insertion of the PRO DNA using ligation methods such as described in Sambrook et al., *supra*. The resulting vector is called pRK5-PRO.

- 15 In one embodiment, the selected host cells may be 293 cells. Human 293 cells (ATCC CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, nutrient components and/or antibiotics. About 10 μ g pRK5-PRO DNA is mixed with about 1 μ g DNA encoding the VA RNA gene [Thimmappaya et al., *Cell*, 31:543 (1982)] and dissolved in 500 μ l of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M CaCl_2 . To this mixture is added, dropwise, 500 μ l of 50 mM HEPES (pH 7.35), 280 mM NaCl, 1.5 mM NaPO_4 , and a precipitate is allowed to form for 10 minutes at 25°C. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37°C. The culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

- 25 Approximately 24 hours after the transfections, the culture medium is removed and replaced with culture medium (alone) or culture medium containing 200 $\mu\text{Ci/ml}$ ^{35}S -cysteine and 200 $\mu\text{Ci/ml}$ ^{35}S -methionine. After a 12 hour incubation, the conditioned medium is collected, concentrated on a spin filter, and loaded onto a 15% SDS gel. The processed gel may be dried and exposed to film for a selected period of time to reveal the presence of PRO polypeptide. The cultures containing transfected cells may undergo further incubation (in serum free medium) and the medium is tested in selected bioassays.

- 30 In an alternative technique, PRO may be introduced into 293 cells transiently using the dextran sulfate method described by Sompayrac et al., *Proc. Natl. Acad. Sci.*, 12:7575 (1981). 293 cells are grown to maximal density in a spinner flask and 700 μ g pRK5-PRO DNA is added. The cells are first concentrated from the spinner flask by centrifugation and washed with PBS. The DNA-dextran precipitate is incubated on the cell pellet for four hours. The cells are treated with 20% glycerol for 90 seconds, washed with tissue culture medium, and re-introduced into the spinner flask containing tissue culture medium, 5 $\mu\text{g/ml}$ bovine insulin and 35 0.1 $\mu\text{g/ml}$ bovine transferrin. After about four days, the conditioned media is centrifuged and filtered to remove cells and debris. The sample containing expressed PRO can then be concentrated and purified by any selected method, such as dialysis and/or column chromatography.

In another embodiment, PRO can be expressed in CHO cells. The pRK5-PRO can be transfected into CHO cells using known reagents such as CaPO₄ or DEAE-dextran. As described above, the cell cultures can be incubated, and the medium replaced with culture medium (alone) or medium containing a radiolabel such as ³⁵S-methionine. After determining the presence of PRO polypeptide, the culture medium may be replaced with serum free medium. Preferably, the cultures are incubated for about 6 days, and then the conditioned medium is harvested. The medium containing the expressed PRO can then be concentrated and purified by any selected method.

Epitope-tagged PRO may also be expressed in host CHO cells. The PRO may be subcloned out of the pRK5 vector. The subclone insert can undergo PCR to fuse in frame with a selected epitope tag such as a poly-his tag into a Baculovirus expression vector. The poly-his tagged PRO insert can then be subcloned into a SV40 driven vector containing a selection marker such as DHFR for selection of stable clones. Finally, the CHO cells can be transfected (as described above) with the SV40 driven vector. Labeling may be performed, as described above, to verify expression. The culture medium containing the expressed poly-His tagged PRO can then be concentrated and purified by any selected method, such as by Ni²⁺-chelate affinity chromatography.

PRO may also be expressed in CHO and/or COS cells by a transient expression procedure or in CHO cells by another stable expression procedure.

Stable expression in CHO cells is performed using the following procedure. The proteins are expressed as an IgG construct (immunoadhesin), in which the coding sequences for the soluble forms (e.g. extracellular domains) of the respective proteins are fused to an IgG1 constant region sequence containing the hinge, CH2 and CH2 domains and/or is a poly-His tagged form.

Following PCR amplification, the respective DNAs are subcloned in a CHO expression vector using standard techniques as described in Ausubel et al., Current Protocols of Molecular Biology, Unit 3.16, John Wiley and Sons (1997). CHO expression vectors are constructed to have compatible restriction sites 5' and 3' of the DNA of interest to allow the convenient shuttling of cDNA's. The vector used expression in CHO cells is as described in Lucas et al., Nucl. Acids Res. 24:9 (1774-1779 (1996), and uses the SV40 early promoter/enhancer to drive expression of the cDNA of interest and dihydrofolate reductase (DHFR). DHFR expression permits selection for stable maintenance of the plasmid following transfection.

Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect[®] (Quiagen), Dosper[®] or Fugene[®] (Boehringer Mannheim). The cells are grown as described in Lucas et al., supra. Approximately 3 x 10⁷ cells are frozen in an ampule for further growth and production as described below.

The ampules containing the plasmid DNA are thawed by placement into water bath and mixed by vortexing. The contents are pipetted into a centrifuge tube containing 10 mLs of media and centrifuged at 1000 rpm for 5 minutes. The supernatant is aspirated and the cells are resuspended in 10 mL of selective media (0.2 μ m filtered PS20 with 5% 0.2 μ m diafiltered fetal bovine serum). The cells are then aliquoted into a 100 mL spinner containing 90 mL of selective media. After 1-2 days, the cells are transferred into a 250 mL spinner filled with 150 mL selective growth medium and incubated at 37°C. After another 2-3 days, 250 mL, 500 mL and 2000 mL spinners are seeded with 3 x 10⁵ cells/mL. The cell media is exchanged with fresh media by

centrifugation and resuspension in production medium. Although any suitable CHO media may be employed, a production medium described in U.S. Patent No. 5,122,469, issued June 16, 1992 may actually be used. A 3L production spinner is seeded at 1.2×10^6 cells/mL. On day 0, the cell number pH is determined. On day 1, the spinner is sampled and sparging with filtered air is commenced. On day 2, the spinner is sampled, the temperature shifted to 33°C, and 30 mL of 500 g/L glucose and 0.6 mL of 10% antifoam (e.g., 35% polydimethylsiloxane emulsion, Dow Corning 365 Medical Grade Emulsion) taken. Throughout the production, the pH is adjusted as necessary to keep it at around 7.2. After 10 days, or until the viability dropped below 70%, the cell culture is harvested by centrifugation and filtering through a 0.22 μ m filter. The filtrate was either stored at 4°C or immediately loaded onto columns for purification.

For the poly-His tagged constructs, the proteins are purified using a Ni-NTA column (Qiagen). Before purification, imidazole is added to the conditioned media to a concentration of 5 mM. The conditioned media is pumped onto a 6 ml Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 M NaCl and 5 mM imidazole at a flow rate of 4-5 ml/min. at 4°C. After loading, the column is washed with additional equilibration buffer and the protein eluted with equilibration buffer containing 0.25 M imidazole. The highly purified protein is subsequently desalted into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 ml G25 Superfine (Pharmacia) column and stored at -80°C.

Immunoadhesin (Fc-containing) constructs are purified from the conditioned media as follows. The conditioned medium is pumped onto a 5 ml Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column is washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein is immediately neutralized by collecting 1 ml fractions into tubes containing 275 μ L of 1 M Tris buffer, pH 9. The highly purified protein is subsequently desalted into storage buffer as described above for the poly-His tagged proteins. The homogeneity is assessed by SDS polyacrylamide gels and by N-terminal amino acid sequencing by Edman degradation.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

25 EXAMPLE 142: Expression of PRO in Yeast

The following method describes recombinant expression of PRO in yeast.

First, yeast expression vectors are constructed for intracellular production or secretion of PRO from the ADH2/GAPDH promoter. DNA encoding PRO and the promoter is inserted into suitable restriction enzyme sites in the selected plasmid to direct intracellular expression of PRO. For secretion, DNA encoding PRO can be cloned into the selected plasmid, together with DNA encoding the ADH2/GAPDH promoter, a native PRO signal peptide or other mammalian signal peptide, or, for example, a yeast alpha-factor or invertase secretory signal/leader sequence, and linker sequences (if needed) for expression of PRO.

Yeast cells, such as yeast strain AB110, can then be transformed with the expression plasmids described above and cultured in selected fermentation media. The transformed yeast supernatants can be analyzed by precipitation with 10% trichloroacetic acid and separation by SDS-PAGE, followed by staining of the gels with Coomassie Blue stain.

Recombinant PRO can subsequently be isolated and purified by removing the yeast cells from the fermentation medium by centrifugation and then concentrating the medium using selected cartridge filters. The concentrate containing PRO may further be purified using selected column chromatography resins.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

5 EXAMPLE 143: Expression of PRO in Baculovirus-Infected Insect Cells

The following method describes recombinant expression of PRO in Baculovirus-infected insect cells.

The sequence coding for PRO is fused upstream of an epitope tag contained within a baculovirus expression vector. Such epitope tags include poly-his tags and immunoglobulin tags (like Fc regions of IgG). A variety of plasmids may be employed, including plasmids derived from commercially available plasmids such as pVL1393 (Novagen). Briefly, the sequence encoding PRO or the desired portion of the coding sequence of PRO such as the sequence encoding the extracellular domain of a transmembrane protein or the sequence encoding the mature protein if the protein is extracellular is amplified by PCR with primers complementary to the 5' and 3' regions. The 5' primer may incorporate flanking (selected) restriction enzyme sites. The product is then digested with those selected restriction enzymes and subcloned into the expression vector.

15 Recombinant baculovirus is generated by co-transfecting the above plasmid and BaculoGold™ virus DNA (Pharmingen) into *Spodoptera frugiperda* ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL). After 4 - 5 days of incubation at 28°C, the released viruses are harvested and used for further amplifications. Viral infection and protein expression are performed as described by O'Reilley et al., Baculovirus expression vectors: A Laboratory Manual, Oxford: Oxford University Press (1994).

20 Expressed poly-his tagged PRO can then be purified, for example, by Ni²⁺-chelate affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by Rupert et al., Nature, 362:175-179 (1993). Briefly, Sf9 cells are washed, resuspended in sonication buffer (25 mL Hepes, pH 7.9; 12.5 mM MgCl₂; 0.1 mM EDTA; 10% glycerol; 0.1% NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the supernatant is diluted 50-fold in loading buffer (50 mM phosphate, 300 mM NaCl, 10% glycerol, pH 7.8) and filtered through a 0.45 μm filter. A Ni²⁺-NTA agarose column (commercially available from Qiagen) is prepared with a bed volume of 5 mL, washed with 25 mL of water and equilibrated with 25 mL of loading buffer. The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed to baseline A₂₈₀ with loading buffer, at which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50 mM phosphate; 300 mM NaCl, 10% glycerol, pH 6.0), which elutes nonspecifically bound protein. After reaching A₂₈₀ baseline again, the column is developed with a 0 to 500 mM Imidazole gradient in the secondary wash buffer. One mL fractions are collected and analyzed by SDS-PAGE and silver staining or Western blot with Ni²⁺-NTA-conjugated to alkaline phosphatase (Qiagen). Fractions containing the eluted His₁₀-tagged PRO are pooled and dialyzed against loading buffer.

35 Alternatively, purification of the IgG tagged (or Fc tagged) PRO can be performed using known chromatography techniques, including for instance, Protein A or protein G column chromatography.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 144: Preparation of Antibodies that Bind PRO

This example illustrates preparation of monoclonal antibodies which can specifically bind PRO.

Techniques for producing the monoclonal antibodies are known in the art and are described, for instance, in Goding, *supra*. Immunogens that may be employed include purified PRO, fusion proteins containing PRO, and cells expressing recombinant PRO on the cell surface. Selection of the immunogen can be made by the skilled artisan without undue experimentation.

Mice, such as Balb/c, are immunized with the PRO immunogen emulsified in complete Freund's adjuvant and injected subcutaneously or intraperitoneally in an amount from 1-100 micrograms. Alternatively, the immunogen is emulsified in MPL-TDM adjuvant (Ribi Immunochemical Research, Hamilton, MT) and injected into the animal's hind foot pads. The immunized mice are then boosted 10 to 12 days later with additional immunogen emulsified in the selected adjuvant. Thereafter, for several weeks, the mice may also be boosted with additional immunization injections. Serum samples may be periodically obtained from the mice by retro-orbital bleeding for testing in ELISA assays to detect anti-PRO antibodies.

After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a final intravenous injection of PRO. Three to four days later, the mice are sacrificed and the spleen cells are harvested. The spleen cells are then fused (using 35% polyethylene glycol) to a selected murine myeloma cell line such as P3X63AgU.1, available from ATCC, No. CRL 1597. The fusions generate hybridoma cells which can then be plated in 96 well tissue culture plates containing HAT (hypoxanthine, aminopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids, and spleen cell hybrids.

The hybridoma cells will be screened in an ELISA for reactivity against PRO. Determination of "positive" hybridoma cells secreting the desired monoclonal antibodies against PRO is within the skill in the art.

The positive hybridoma cells can be injected intraperitoneally into syngeneic Balb/c mice to produce ascites containing the anti-PRO monoclonal antibodies. Alternatively, the hybridoma cells can be grown in tissue culture flasks or roller bottles. Purification of the monoclonal antibodies produced in the ascites can be accomplished using ammonium sulfate precipitation, followed by gel exclusion chromatography. Alternatively, affinity chromatography based upon binding of antibody to protein A or protein G can be employed.

EXAMPLE 145: Purification of PRO Polypeptides Using Specific Antibodies

Native or recombinant PRO polypeptides may be purified by a variety of standard techniques in the art of protein purification. For example, pro-PRO polypeptide, mature PRO polypeptide, or pre-PRO polypeptide is purified by immunoaffinity chromatography using antibodies specific for the PRO polypeptide of interest. In general, an immunoaffinity column is constructed by covalently coupling the anti-PRO polypeptide antibody to an activated chromatographic resin.

Polyclonal immunoglobulins are prepared from immune sera either by precipitation with ammonium sulfate or by purification on immobilized Protein A (Pharmacia LKB Biotechnology, Piscataway, N.J.). Likewise, monoclonal antibodies are prepared from mouse ascites fluid by ammonium sulfate precipitation or chromatography on immobilized Protein A. Partially purified immunoglobulin is covalently attached to a chromatographic resin such as CnBr-activated SEPHAROSE™ (Pharmacia LKB Biotechnology). The antibody

is coupled to the resin, the resin is blocked, and the derivative resin is washed according to the manufacturer's instructions.

Such an immunoaffinity column is utilized in the purification of PRO polypeptide by preparing a fraction from cells containing PRO polypeptide in a soluble form. This preparation is derived by solubilization of the whole cell or of a subcellular fraction obtained via differential centrifugation by the addition of detergent or by other methods well known in the art. Alternatively, soluble PRO polypeptide containing a signal sequence may be secreted in useful quantity into the medium in which the cells are grown.

A soluble PRO polypeptide-containing preparation is passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of PRO polypeptide (*e.g.*, high ionic strength buffers in the presence of detergent). Then, the column is eluted under conditions that disrupt antibody/PRO polypeptide binding (*e.g.*, a low pH buffer such as approximately pH 2-3, or a high concentration of a chaotrope such as urea or thiocyanate ion), and PRO polypeptide is collected.

EXAMPLE 146: Drug Screening

This invention is particularly useful for screening compounds by using PRO polypeptides or binding fragment thereof in any of a variety of drug screening techniques. The PRO polypeptide or fragment employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the PRO polypeptide or fragment. Drugs are screened against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between PRO polypeptide or a fragment and the agent being tested. Alternatively, one can examine the diminution in complex formation between the PRO polypeptide and its target cell or target receptors caused by the agent being tested.

Thus, the present invention provides methods of screening for drugs or any other agents which can affect a PRO polypeptide-associated disease or disorder. These methods comprise contacting such an agent with an PRO polypeptide or fragment thereof and assaying (i) for the presence of a complex between the agent and the PRO polypeptide or fragment, or (ii) for the presence of a complex between the PRO polypeptide or fragment and the cell, by methods well known in the art. In such competitive binding assays, the PRO polypeptide or fragment is typically labeled. After suitable incubation, free PRO polypeptide or fragment is separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of the particular agent to bind to PRO polypeptide or to interfere with the PRO polypeptide/cell complex.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to a polypeptide and is described in detail in WO 84/03564, published on September 13, 1984. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. As applied to a PRO polypeptide, the peptide test compounds are reacted with PRO polypeptide and washed. Bound PRO polypeptide is detected by methods well known in the art. Purified PRO polypeptide can also be coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the peptide and immobilize it on the

solid support.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding PRO polypeptide specifically compete with a test compound for binding to PRO polypeptide or fragments thereof. In this manner, the antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with PRO polypeptide.

5

EXAMPLE 147: Rational Drug Design

The goal of rational drug design is to produce structural analogs of biologically active polypeptide of interest (*i.e.*, a PRO polypeptide) or of small molecules with which they interact, *e.g.*, agonists, antagonists, or inhibitors. Any of these examples can be used to fashion drugs which are more active or stable forms of the PRO polypeptide or which enhance or interfere with the function of the PRO polypeptide *in vivo* (*c.f.*, Hodgson, Bio/Technology, 9: 19-21 (1991)).

In one approach, the three-dimensional structure of the PRO polypeptide, or of an PRO polypeptide-inhibitor complex, is determined by x-ray crystallography, by computer modeling or, most typically, by a combination of the two approaches. Both the shape and charges of the PRO polypeptide must be ascertained to elucidate the structure and to determine active site(s) of the molecule. Less often, useful information regarding the structure of the PRO polypeptide may be gained by modeling based on the structure of homologous proteins. In both cases, relevant structural information is used to design analogous PRO polypeptide-like molecules or to identify efficient inhibitors. Useful examples of rational drug design may include molecules which have improved activity or stability as shown by Braxton and Wells, Biochemistry, 31:7796-7801 (1992) or which act as inhibitors, agonists, or antagonists of native peptides as shown by Athauda *et al.*, J. Biochem., 113:742-746 (1993).

It is also possible to isolate a target-specific antibody, selected by functional assay, as described above, and then to solve its crystal structure. This approach, in principle, yields a pharmacore upon which subsequent drug design can be based. It is possible to bypass protein crystallography altogether by generating anti-idiotypic antibodies (anti-ids) to a functional, pharmacologically active antibody. As a mirror image of a mirror image, the binding site of the anti-ids would be expected to be an analog of the original receptor. The anti-id could then be used to identify and isolate peptides from banks of chemically or biologically produced peptides. The isolated peptides would then act as the pharmacore.

By virtue of the present invention, sufficient amounts of the PRO polypeptide may be made available to perform such analytical studies as X-ray crystallography. In addition, knowledge of the PRO polypeptide amino acid sequence provided herein will provide guidance to those employing computer modeling techniques in place of or in addition to x-ray crystallography.

35

Deposit of Material

The following materials have been deposited with the American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209, USA (ATCC):

Table 2

| <u>5</u> | <u>Material</u> | <u>ATCC Dep. No.</u> | <u>Deposit Date</u> |
|----------|-----------------|----------------------|---------------------|
| | DNA16422-1209 | 209929 | June 2, 1998 |
| | DNA16435-1208 | 209930 | June 2, 1998 |
| | DNA21624-1391 | 209917 | June 2, 1998 |
| | DNA23334-1392 | 209918 | June 2, 1998 |
| 10 | DNA26288-1239 | 209792 | April 21, 1998 |
| | DNA26843-1389 | 203099 | August 4, 1998 |
| | DNA26844-1394 | 209926 | June 2, 1998 |
| | DNA30862-1396 | 209920 | June 2, 1998 |
| | DNA35680-1212 | 209790 | April 21, 1998 |
| 15 | DNA40621-1440 | 209922 | June 2, 1998 |
| | DNA44161-1434 | 209907 | May 27, 1998 |
| | DNA44694-1500 | 203114 | August 11, 1998 |
| | DNA45495-1550 | 203156 | August 25, 1998 |
| | DNA47361-1154 | 209431 | November 7, 1997 |
| 20 | DNA47394-1572 | 203109 | August 11, 1998 |
| | DNA48320-1433 | 209904 | May 27, 1998 |
| | DNA48334-1435 | 209924 | June 2, 1998 |
| | DNA48606-1479 | 203040 | July 1, 1998 |
| | DNA49141-1431 | 203003 | June 23, 1998 |
| 25 | DNA49142-1430 | 203002 | June 23, 1998 |
| | DNA49143-1429 | 203013 | June 23, 1998 |
| | DNA49647-1398 | 209919 | June 2, 1998 |
| | DNA49819-1439 | 209931 | June 2, 1998 |
| | DNA49820-1427 | 209932 | June 2, 1998 |
| 30 | DNA49821-1562 | 209981 | June 16, 1998 |
| | DNA52192-1369 | 203042 | July 1, 1998 |
| | DNA52598-1518 | 203107 | August 11, 1998 |
| | DNA53913-1490 | 203162 | August 25, 1998 |
| | DNA53978-1443 | 209983 | June 16, 1998 |
| 35 | DNA53996-1442 | 209921 | June 2, 1998 |
| | DNA56041-1416 | 203012 | June 23, 1998 |
| | DNA56047-1456 | 209948 | June 9, 1998 |
| | DNA56050-1455 | 203011 | June 23, 1998 |
| | DNA56110-1437 | 203113 | August 11, 1998 |
| 40 | DNA56113-1378 | 203049 | July 1, 1998 |
| | DNA56410-1414 | 209923 | June 2, 1998 |
| | DNA56436-1448 | 209902 | May 27, 1998 |
| | DNA56855-1447 | 203004 | June 23, 1998 |
| | DNA56859-1445 | 203019 | June 23, 1998 |
| 45 | DNA56860-1510 | 209952 | June 9, 1998 |
| | DNA56865-1491 | 203022 | June 23, 1998 |
| | DNA56866-1342 | 203023 | June 23, 1998 |
| | DNA56868-1209 | 203024 | June 23, 1998 |
| | DNA56869-1545 | 203161 | August 25, 1998 |
| 50 | DNA56870-1492 | 209925 | June 2, 1998 |
| | DNA57033-1403 | 209905 | May 27, 1998 |
| | DNA57037-1444 | 209903 | May 27, 1998 |
| | DNA57129-1413 | 209977 | June 16, 1998 |

| | | | |
|----|---------------|--------|-----------------|
| | DNA57690-1374 | 209950 | June 9, 1998 |
| | DNA57693-1424 | 203008 | June 23, 1998 |
| | DNA57694-1341 | 203017 | June 23, 1998 |
| | DNA57695-1340 | 203006 | June 23, 1998 |
| | DNA57699-1412 | 203020 | June 23, 1998 |
| 5 | DNA57702-1476 | 209951 | June 9, 1998 |
| | DNA57704-1452 | 209953 | June 9, 1998 |
| | DNA57708-1411 | 203021 | June 23, 1998 |
| | DNA57710-1451 | 203048 | July 1, 1998 |
| | DNA57711-1501 | 203047 | July 1, 1998 |
| 10 | DNA57827-1493 | 203045 | July 1, 1998 |
| | DNA57834-1339 | 209954 | June 9, 1998 |
| | DNA57836-1338 | 203025 | June 23, 1998 |
| | DNA57838-1337 | 203014 | June 23, 1998 |
| | DNA57844-1410 | 203010 | June 23, 1998 |
| 15 | DNA58721-1475 | 203110 | August 11, 1998 |
| | DNA58723-1588 | 203133 | August 18, 1998 |
| | DNA58737-1473 | 203136 | August 18, 1998 |
| | DNA58743-1609 | 203154 | August 25, 1998 |
| | DNA58846-1409 | 209957 | June 9, 1998 |
| 20 | DNA58848-1472 | 209955 | June 9, 1998 |
| | DNA58849-1494 | 209958 | June 9, 1998 |
| | DNA58850-1495 | 209956 | June 9, 1998 |
| | DNA58853-1423 | 203016 | June 23, 1998 |
| | DNA58855-1422 | 203018 | June 23, 1998 |
| 25 | DNA59205-1421 | 203009 | June 23, 1998 |
| | DNA59211-1450 | 209960 | June 9, 1998 |
| | DNA59213-1487 | 209959 | June 9, 1998 |
| | DNA59214-1449 | 203046 | July 1, 1998 |
| | DNA59215-1425 | 209961 | June 9, 1998 |
| 30 | DNA59220-1514 | 209962 | June 9, 1998 |
| | DNA59488-1603 | 203157 | August 25, 1998 |
| | DNA59493-1420 | 203050 | July 1, 1998 |
| | DNA59497-1496 | 209941 | June 4, 1998 |
| | DNA59588-1571 | 203106 | August 11, 1998 |
| 35 | DNA59603-1419 | 209944 | June 9, 1998 |
| | DNA59605-1418 | 203005 | June 23, 1998 |
| | DNA59606-1471 | 209945 | June 9, 1998 |
| | DNA59607-1497 | 209957 | June 9, 1998 |
| | DNA59609-1470 | 209963 | June 9, 1998 |
| 40 | DNA59610-1559 | 209990 | June 16, 1998 |
| | DNA59612-1466 | 209947 | June 9, 1998 |
| | DNA59613-1417 | 203007 | June 23, 1998 |
| | DNA59616-1465 | 209991 | June 16, 1998 |
| | DNA59619-1464 | 203041 | July 1, 1998 |
| 45 | DNA59620-1463 | 209989 | June 16, 1998 |
| | DNA59625-1498 | 209992 | June 17, 1998 |
| | DNA59767-1489 | 203108 | August 11, 1998 |
| | DNA59776-1600 | 203128 | August 18, 1998 |
| | DNA59777-1480 | 203111 | August 11, 1998 |
| 50 | DNA59820-1549 | 203129 | August 18, 1998 |
| | DNA59827-1426 | 203089 | August 4, 1998 |
| | DNA59828-1608 | 203158 | August 25, 1998 |
| | DNA59838-1462 | 209976 | June 16, 1998 |
| | DNA59839-1461 | 209988 | June 16, 1998 |
| 55 | DNA59841-1460 | 203044 | July 1, 1998 |
| | DNA59842-1502 | 209982 | June 16, 1998 |

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|----|---------------|--------|--------------------|
| | DNA59846-1503 | 209978 | June 16, 1998 |
| | DNA59847-1511 | 203098 | August 4, 1998 |
| | DNA59848-1512 | 203088 | August 4, 1998 |
| | DNA59849-1504 | 209986 | June 16, 1998 |
| | DNA59853-1505 | 209985 | June 16, 1998 |
| 5 | DNA59854-1459 | 209974 | June 16, 1998 |
| | DNA60283-1484 | 203043 | July 1, 1998 |
| | DNA60615-1483 | 209980 | June 16, 1998 |
| | DNA60619-1482 | 209993 | June 16, 1998 |
| | DNA60621-1516 | 203091 | August 4, 1998 |
| 10 | DNA60622-1525 | 203090 | August 4, 1998 |
| | DNA60625-1507 | 209975 | June 16, 1998 |
| | DNA60627-1508 | 203092 | August 4, 1998 |
| | DNA60629-1481 | 209979 | June 16, 1998 |
| | DNA61755-1554 | 203112 | August 11, 1998 |
| 15 | DNA61873-1574 | 203132 | August 18, 1998 |
| | DNA62814-1521 | 203093 | August 4, 1998 |
| | DNA62872-1509 | 203100 | August 4, 1998 |
| | DNA62876-1517 | 203095 | August 4, 1998 |
| | DNA62881-1515 | 203096 | August 4, 1998 |
| 20 | DNA64852-1589 | 203127 | August 18, 1998 |
| | DNA64884-1527 | 203155 | August 25, 1998 |
| | DNA64890-1612 | 203131 | August 18, 1998 |
| | DNA65412-1523 | 203094 | August 4, 1998 |
| | DNA66308-1537 | 203159 | August 25, 1998 |
| 25 | DNA66309-1538 | 203235 | September 15, 1998 |
| | DNA67004-1614 | 203115 | August 11, 1998 |
| | DNA68869-1610 | 203164 | August 25, 1998 |
| | DNA68872-1620 | 203160 | August 25, 1998 |
| 30 | DNA71159-1617 | 203135 | August 18, 1998 |

These deposit were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The deposits will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement between Genentech, Inc. and ATCC, which assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC §122 and the Commissioner's rules pursuant thereto (including 37 CFR §1.14 with particular reference to 886 OG 638).

The assignee of the present application has agreed that if a culture of the materials on deposit should die or be lost or destroyed when cultivated under suitable conditions, the materials will be promptly replaced on notification with another of the same. Availability of the deposited material is not to be construed as a license to practice the invention in contravention of the rights granted under the authority of any government in accordance with its patent laws.

The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the construct deposited, since the

deposited embodiment is intended as a single illustration of certain aspects of the invention and any constructs that are functionally equivalent are within the scope of this invention. The deposit of material herein does not constitute an admission that the written description herein contained is inadequate to enable the practice of any aspect of the invention, including the best mode thereof, nor is it to be construed as limiting the scope of the claims to the specific illustrations that it represents. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims.

WHAT IS CLAIMED IS:

1. Isolated nucleic acid having at least 80% sequence identity to a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ

ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422) and Figure 306 (SEQ ID NO:424).

2. The nucleic acid sequence of Claim 1, wherein said nucleotide sequence comprises a nucleotide
- 5 sequence selected from the group consisting of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72),
- 10 Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166),
- 15 Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204),
- 20 Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259),
- 25 Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288),
- 30 Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358),
- 35 Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372),

Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421) and Figure 305 (SEQ ID NO:423).

3. The nucleic acid of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequence selected from the group consisting of the full-length coding sequence of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID

- NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421) or Figure 305 (SEQ ID NO:423).
4. Isolated nucleic acid which comprises the full-length coding sequence of the DNA deposited under any ATCC accession number shown in Table 2.
5. A vector comprising the nucleic acid of Claim 1.
6. The vector of Claim 5 operably linked to control sequences recognized by a host cell transformed with the vector.
7. A host cell comprising the vector of Claim 5.
8. The host cell of Claim 7 wherein said cell is a CHO cell.
9. The host cell of Claim 7 wherein said cell is an *E. coli*.
10. The host cell of Claim 7 wherein said cell is a yeast cell.
11. A process for producing a PRO polypeptides comprising culturing the host cell of Claim 7 under conditions suitable for expression of said PRO polypeptide and recovering said PRO polypeptide from the cell culture.
12. Isolated PRO polypeptide having at least 80% sequence identity to an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68

(SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422) and Figure 306 (SEQ ID NO:424).

13. Isolated PRO polypeptide having at least 80% sequence identity to the amino acid sequence encoded by a nucleic acid molecule deposited under any ATCC accession number shown in Table 2.

14. A chimeric molecule comprising a polypeptide according to Claim 12 fused to a heterologous amino acid sequence.

15. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is an epitope tag sequence.
16. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is a Fc region of an immunoglobulin.
- 5 17. An antibody which specifically binds to a PRO polypeptide according to Claim 12.
18. The antibody of Claim 17 wherein said antibody is a monoclonal antibody.
- 10 19. The antibody of Claim 17 wherein said antibody is a humanized antibody.
20. The antibody of Claim 17 wherein said antibody is an antibody fragment.
21. An isolated nucleic acid molecule which has at least 80% sequence identity to a nucleic acid
15 which comprises a nucleotide sequence selected from the group consisting of that shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure
20 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID
25 NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure
30 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID
35 NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure

191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421) and Figure 305 (SEQ ID NO:423).

22. An isolated nucleic acid molecule which has at least 80% sequence identity to the full-length coding sequence of a nucleotide sequence selected from the group consisting of that shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID

- NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421) and Figure 305 (SEQ ID NO:423).
- 20 23. An isolated extracellular domain of of PRO polypeptide.
24. An isolated PRO polypeptide lacking its associated signal peptide.
25. An isolated polypeptide having at least about 80% amino acid sequence identity to an
25 extracellular domain of of PRO polypeptide.
26. An isolated polypeptide having at least about 80% amino acid sequence identity to a PRO
polypeptide lacking its associated signal peptide.

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FIGURE 1

CGGACGCGTGGGTGCGAGGCGAAGGTGACCGGGGACCGAGCATTTAGATCTGCTCGGTAGA
CCTGGTGCACCACCACCATGTTGGCTGCAAGGCTGGTGTGTCTCCGGACACTACCTTCTAGG
GTTTTCCACCCAGCTTTACCAAGGCCTCCCCTGTTGTGAAGAATTCCATCACGAAGAATCA
ATGGCTGTAAACACCTAGCAGGGAATATGCCACCAAAACAAGAATTGGGATCCGGCGTGGGA
GAACTGGCCAAGAACTCAAAGAGGCAGCATTGGAACCATCGATGGAAAAAATATTTAAAATT
GATCAGATGGGAAGATGGTTTGTGTGCTGGAGGGGCTGCTGTTGGTCTTGGAGCATTGTGCTA
CTATGGCTTGGGACTGTCTAATGAGATTGGAGCTATTGAAAAGGCTGTAATTTGGCCTCAGT
ATGTCAAGGATAGAATTCATTCCACCTATATGTACTTAGCAGGGAGTATTGGTTTAAACAGCT
TTGTCTGCCATAGCAATCAGCAGAACGCCTGTTCTCATGAACTTCATGATGAGAGGCTCTTG
GGTGACAATTGGTGTGACCTTTGCAGCCATGGTTGGAGCTGGAATGCTGGTACGATCAATAC
CATATGACCAGAGCCCAGGCCCAAAGCATCTTGCTTGGTTGCTACATTCTGGTGTGATGGGT
GCAGTGGTGGCTCCTCTGACAATATTAGGGGGTCTCTTCTCATCAGAGCTGCATGGTACAC
AGCTGGCATTGTGGGAGGCCTCTCCACTGTGGCCATGTGTGCGCCAGTGAAAAGTTTCTGA
ACATGGGTGCACCCCTGGGAGTGGGCCTGGGTCTCGTCTTTGTGTCCTCATTGGGATCTATG
TTTCTTCCACCTACCACCGTGGCTGGTGCCACTCTTTACTCAGTGGCAATGTACGGTGGATT
AGTTCTTTTTCAGCATGTTCCCTTCTGTATGATACCCAGAAAGTAATCAAGCGTGCAGAAGTAT
CACCAATGTATGGAGTTCAAAAATATGATCCCATTAACTCGATGCTGAGTATCTACATGGAT
ACATTAAATATATTTATGCGAGTTGCAACTATGCTGGCAACTGGAGGCAACAGAAAGAAATG
AAGTGACTCAGCTTCTGGCTTCTCTGCTACATCAAATATCTTGTTTAATGGGGCAGATATGC
ATTAAATAGTTTGTACAAGCAGCTTTCGTTGAAGTTTAGAAGATAAGAAACATGTCATCATA
TTTAAATGTTCCGGTAATGTGATGCCTCAGGTCTGCCTTTTTTTCTGGAGAATAAATGCAGT
AATCCTCTCCCAAATAAGCACACACATTTTCAATTCTCATGTTTGAGTGATTTTAAAATGTT
TTGGTGAATGTGAAAACATAAGTTTGTGTGATGAGAATGTAAGTCTTTTTTCTACTTTAAAA
TTTAGTAGGTTCACTGAGTAACATAAAATTTAGCAAACCTGTGTTTGCAATTTTTTTTGGAGT
GCAGAATATTGTAATTAATGTCATAAGTGATTTGGAGCTTTGGTAAAGGGACCAGAGAGAAG
GAGTCACCTGCAGTCTTTTGTGTTTTTAAATACTTAGAACCTTAGCACTTGTGTTATTGATTA
GTGAGGAGCCAGTAAGAAACATCTGGGTATTTGGAAACAAGTGGTCATTGTTACATTCATTT
GCTGAACTTAACAAAACCTGTTTCATCCTGAAACAGGCACAGGTGATGCATTCTCCTGCTGTTG
CTTCTCAGTGCTCTCTTCCAATATAGATGTGGTCACTGTTTGACTTGTACAGAATGTTAATC
ATACAGAGAATCCTTGATGGAATTATATATGTGTGTTTTACTTTTGAATGTTACAAAAGGAA
ATAACTTTAAACATATTCTCAAGAGAAAATATTCAAAGCATGAAATATGTTGCTTTTTCCAG
AATACAAACAGTATACTCATG

FIGURE 2

MLAARLVCLRTLPSRVFHPAFTKASPVVKNSITKNQWLLTPSREYATKTRIGIRRGRTGQEL
KEAALEPSMEKIFKIDQMGRWVFVAGGAAVGLGALCYGLGLSNEIGAIEKAVIWPQYVKDRI
HSTMYLAGSIGLTALSAIAISRTPVLMNFMMRGSWVTIGVTFAAMVGAGMLVRSIPYDQSP
GPKHLAWLLHSGVMGAVVAPLTIILGGPLLIRAAWYTAGIVGGLSTVAMCAPSEKFLNMGAPL
GVGLGLVVFVSSLGSMFLPPTTVAGATLYSVAMYGGLVLFMSMFLLYDTQKVIKRAEVSPMYGV
QKYDPINSMLSIYMDTLNIFMRVATMLATGGNRKK

FIGURE 3

GAAGGCTGCCTCGCTGGTCCGAATTGGTGGCGCCACGTCCGCCCGTCTCCGCCTTCTGCAT
CGCGGCTTCGGCGGCTTCCACCTAGACACCTAACAGTCGCGGAGCCCGCCGCGTCTGAGGG
GGTCCGCACGGGAGTCGGGCGGTCTTGTGCATCTTGGCTACCTGTGGGTGGAAGATGTCGG
ACATCGGAGACTGGTTCAGGAGCATCCCGGCGATCACGCGCTATTGGTTCGCCGCCACCGTC
GCCGTGCCCTTGGTCGGCAAACCTCGGCCTCATCAGCCCGGCTACCTCTTCTCTGGCCCCGA
AGCCTTCTTTATCGCTTTCAGATTTGGAGGCCAATCACTGCCACCTTTTATTTCCCTGTGG
GTCCAGGAACCTGGATTTCTTTATTTGGTCAATTTATATTTCTTATATCAGTATTTCTACGCGA
CTTGAAACAGGAGCTTTTGATGGGAGGCCAGCAGACTATTTATTCATGCTCCTCTTTAACTG
GATTTGCATCGTGATTACTGGCTTAGCAATGGATATGCAGTTGCTGATGATTCCTCTGATCA
TGTCAGTACTTTATGTCTGGGCCCAGCTGAACAGAGACATGATTGTATCATTTTGGTTTGGGA
ACACGATTTAAGGCCTGCTATTTACCCTGGGTTATCCTTGGATTCAACTATATCATCGGAGG
CTCGGTAATCAATGAGCTTATTGGAAATCTGGTTGGACATCTTTATTTTTCTTAATGTTCA
GATACCCAATGGACTTGGGAGGAAGAAATTTCTATCCACACCTCAGTTTTTGTACCGCTGG
CTGCCCAGTAGGAGAGGAGGAGTATCAGGATTTGGTGTGCCCCCTGCTAGCATGAGGCGAGC
TGCTGATCAGAATGGCGGAGGCGGGAGACACAACCTGGGGCCAGGGCTTTCGACTTGGAGACC
AGTGAAGGGGCGGCTCGGGCAGCCGCTCCTCTCAAGCCACATTTCCCTCCAGTGCTGGGTG
CACTTAACAACCTGCGTTCTGGCTAACACTGTTGGACCTGACCCACACTGAATGTAGTCTTTC
AGTACGAGACAAAGTTTCTTAAATCCCGAAGAAAAATATAAGTGTCCACAAGTTTCACGAT
TCTCATTCAAGTCTTACTGCTGTGAAGAACAATACCAACTGTGCAAAATGCAAACTGCAC
TACATTTTTTGGTGTCTTCTCTTCTCCCCTTTCCGCTCTGAATAATGGGTTTTAGCGGGTCTT
AATCTGCTGGCATTGAGCTGGGGCTGGGTACCAAACCCCTTCCCAAAGGACCTTATCTCTT
TCTTGACACATGCCTCTCTCCCACTTTTCCCAACCCCCACATTTGCAACTAGAAAAAGTTG
CCCATAAAATTGCTCTGCCCTTGACAGGTTCTGTTATTTATTGACTTTTGCCAAGGCTGGTC
ACAACAATCATATTCACGTTATTTTTCCCCTTTTGGTGGCAGAACTGTTACCAATAGGGGGAG
AAGACAGCCACGGATGAAGCGTTTCTCAGCTTTTGAATGCTTCGACTGACATCGCTTGTGTT
AACCCTTTGGCACTCTTCAGATATTTTTTATAAAAAAGTACCCTGAGTTTCATGAGGGCCA
CAGATTGGTTATTAATGAGATACGAGGGTTGGTGTGGTGTGTTGTTTCTGAGCTAAGTGA
TCAAGACTGTAGTGGAGTTGCAGCTAACATGGGTTAGGTTTAAACCATGGGGGATGCACCCC
TTTGCGTTTCATATGTAGCCCTACTGGCTTGTGTAGCTGGAGTAGTTGGGTTGCTTTGTGT
TAGGAGGATCCAGATCATGTTGGCTACAGGGAGATGCTCTCTTGGAGAGTCTGGGCATTG
ATTCCTCATTTCAATCTCATTCTGGATATGTGTTCAATTGAGTAAAGGAGGAGAGCCCTCATA
CGCTATTTAAATGTCACTTTTTTGCCTATCCCCGTTTTTTGGTTCATGTTTCAATTAATTGT
GAGGAAGGCGCAGCTCCTCTCTGCACGTAGATCATTTTTTAAAGCTAATGTAAGCACATCTA
AGGGAATAACATGATTTAAGGTTGAAATGGCTTTAGAATCATTTGGGTTTGAGGGTGTGTTA
TTTTGAGTCATGAATGTACAAGCTCTGTGAATCAGACCAGCTTAAATACCCACACCTTTTTT
TCGTAGGTGGGCTTTTCTATCAGAGCTTGGCTCATAACCAAATAAAGTTTTTTGAAGGCCA
TGGCTTTTACACAGTTATTTTATTTTATGACGTTATCTGAAAGCAGACTGTTAGGAGCAGT
ATTGAGTGGCTGTCACTTTTGGGCAACTAAAAAGGCTTCAAACGTTTTTGATCAGTTTCTT
TTCAGGAAACATTGTGCTCTAACAGTATGACTATTCTTTCCCCACTCTTAAACAGTGTGAT
GTGTGTTATCCTAGGAAATGAGAGTTGGCAAACAACCTTCTCATTTTGAATAGAGTTTGTGTG
TACTTCTCCATATTTAATTTATATGATAAAATAGGTGGGAGAGTCTGAACCTTAACTGTCA
TGTTTTTGTGTTTCTGTGGCCACAATAAAGTTTACTTGTAATTTTAGAGGCCATTACT
CCAATTATGTTGCACGTACACTCATTGTACAGGCGTGGAGACTCATTGTATGTATAAGAATA
TTTCTGACAGTGAGTGACCCGGAGTCTCTGGTGTACCCTCTTACCAGTCAGCTGCCTGCCGAG
CAGTCATTTTTTCTAAAGGTTTACAAGTATTTAGAACTTTTCAAGTTTCAAGGCAAAATGTTT
ATGAAGTTATTCTCTTAAACATGGTTAGGAAGCTGATGACGTTATTGATTTTGTCTGGATT
ATGTTTCTGGAATAATTTTACCAAAACAAGCTATTTGAGTTTTGACTTGACAAGGCAAAACA
TGACAGTGGATTCTCTTTACAAATGGAAAAAAAATCCTTATTTTGTATAAAGGACTTCCC
TTTTTGTAATACTAATCCTTTTTATTGGTAAAAATGTAAATTAATAATGTGCAACTTG

FIGURE 4

MSDIGDWFRSIPAITRYWFAATVAVPLVGKLGGLISPAYLFLWPEAFLYRFQIWRPITATFYF
PVGPGTGFLYLVLNLYFLYQYSTRLETGAFDGRPADYLFMLLFNWICIVITGLAMDMQLLMIP
LIMSVLYVWAQLNRDMIVSFWFGTRFKACYLPWVILGFNYIIIGGSVINELIGNLVGHLYFFL
MFRYPMDLGGRNFLSTPQFLYRWLPSRRGGVSGFGVPPASMRRAADQNGGGGRHNWGQGFRLLGDQ

FIGURE 5

GGGGCCGCGGTCTAGGGCGGCTACGTGTGTTGCCATAGCGACCATTTTGCATTAACTGGTTG
GTAGCTTCTATCCTGGGGGCTGAGCGACTGCGGGCCAGCTCTTCCCCTACTCCCTCTCGGCT
CCTTGTGGCCCAAAGGCCCTAACCGGGGTCCGGCGGTCTGGCCTAGGGATCTTCCCCGTTGCC
CCTTGGGGCGGGATGGCTGCGGAAGAAGAAGACGAGGTGGAGTGGGTAGTGGAGAGCATCG
CGGGGTTCCTGCGAGGCCCAGACTGGTCCATCCCCATCTTGGACTTTGTGGAACAGAAATGT
GAAGTTAACTGCAAAGGAGGGCATGTGATAACTCCAGGAAGCCCAGAGCCGGTGATTTTGGT
GGCCTGTGTTCCCCTTGTTTTTGATGATGAAGAAGAAAGCAAATTGACCTATACAGAGATTG
ATCAGGAATACAAAGAACTAGTTGAAAAGCTGTTAGAAGGTTACCTCAAAGAAATTGGAATT
AATGAAGATCAATTTCAAGAAGCATGCACTTCTCCTCTTGCAAAGACCCATACATCACAGGC
CATTTTGCAACCTGTGTTGGCAGCAGAAGATTTTACTATCTTTAAAGCAATGATGGTCCAGA
AAAACATTGAAATGCAGCTGCAAGCCATTGCAATAATTCAAGAGAGAAATGGTGTATTACCT
GACTGCTTAACCGATGGCTCTGATGTGGTCAGTGACCTTGAACACGAAGAGATGAAAATCCT
GAGGGAAGTTCTTAGAAAATCAAAAGAGGAATATGACCAGGAAGAAGAAAGGAAGAGGAAAA
AACAGTTATCAGAGGCTAAAACAGAAGAGCCACAGTGCATTCCAGTGAAGCTGCAATAATG
AATAATTCCTAAGGGGATGGTGAACATTTTGCACACCCACCCCTCAGAAGTTAAATGCATTT
TGCTAATCAGTCAATAGAACCTTTGGGAAGAAAAGTGGAAAGGTCTGAAACTTCCTCCCTCC
CACAAAAGGCCTGAAGATTCCTGGCTTAGAGCATGCGAGCATTGAAGGACCAATAGCAAAC
TTATCAGTACTTGGAACAGAAGAACTTCGGCAACGAGAACACTATCTCAAGCAGAAGAGAGA
TAAGTTGATGTCCATGAGAAAGGATATGAGGACTAAACAGATACAAAATATGGAGCAGAAAG
GAAAACCCACTGGGGAGGTAGAGGAAATGACAGAGAAACCAGAAATGACAGCAGAGGAGAAG
CAAACATTACTAAAGAGGAGATTGCTTGCAGAGAAACTCAAAGAAGAAGTTATTAATAAGTA
ATAATTAAGAACAATTTAACAAAATGGAAGTTCAAATTGTCTTAAAAATAAATTATTTAGTC
CTTACACTG

FIGURE 6

MAAEEDEVEWVVESIAGFLRGPDWSIPILDFVEQCEVNCKGGHVITPGSPEPVILVACVP
LVFDDEESKLTYTEIHQEYKELVEKLLEGYLKEIGINEDQFQEAactsSPLAKTHTSQAILQP
VLAAEDFTIFKAMMVQKNIEMLQAIRIIQERNGLVPDCLTDGSDVVSdleHEEMKILREVL
RKSKEEYDQEEERKRKKQLSEAKTEEPTVHSSEAAIMNNSQGDGEHFAHPPSEVKMHFANQS
IEPLGRKVERSETSSLPQKGLKIPGLEHASIEGP IANLSVLGTEELRQREHYLKQKRDKLMS
MRKDMRTKQIQNMEQKGKPTGEVEEMTEKPEMTAEEKQTLLKRRLLAeKLKEEVINK

FIGURE 7

GGGCACAGCACATGTGAAGTTTTTGATGATGAAGAAGA?AGCAAATTGACCTATACAGAGAT
TCATCAGGAATACAAAGAACTAGTTGAAAAGCTGTTAGAAGGTTACCTCAAAGAAATTGGAA
TTAATGAAGATCAATTTCAAGAAGCATGCACCTTCTCCTCTTGCAAAGACCCATACATCACAG
GCCATTTTTGCAACCTGTGTTGGCAGCAGAAGATTTTACTATCTTTAAAGCAATGATGGTCC
AGAAAAACATTGAAATGCAGCTGCAAGCCATTGAATAATTCAAGAGAGAAATGGTGTATTA
CCTGACTGCTTAACCGATGGCTCTGATGTGGTCAGTGACCTTGAACACGAAGAGATGAAAAT
CCTGAGGGAAGTTCTTAGAAAATCAAAAAGAGGAATATGACCAGGAA

FIGURE 8

GCGTGGTTTTTGTCTGCAATAGGCGGCTTAGAGGGAGGGGCTTTTTCGCCTATACCTACTG
TAGCTTCTCCACGTATGGACCCTAAAGGCTACTGCTGCTACTACGGGGCTAGACAGTTACTG
TCTCAGCTCTAGGATGTGCGTTCTTCCACTAGAAGCTCTTCTGAGGGAGGTAATTA AAAAAC
AGTGGAAATGGAAAAACAGTGCTGTAGTCATCCTGTAATATGCTCCTTGTC AACAATGTATAC
ATTCTGCTAGGTGCCATATTCATTGCTTTAAGCTCAAGTCGCATCTTACTAGTGAAGTATT
CTGCCAATGAAGAAAAACAAGTATGATTATCTTCCAAC TACTGTGAATGTGTGCTCAGAACTG
GTGAAGCTAGTTTTCTGTGTGCTTGTGTCA TTTCTGTGTTATAAAGAAAGATCATCAAAGTAG
AAATTTGAAATATGCTTCCTGGAAGGAATTCCTGATTT CATGAAGTGGTCCATTCCTGCCT
TTCTTTATTTCTTGGA TAACTTGATTGTCTTCTATGTCTCTGCTCTATCTTCAACCAGCCATG
GCTGTTATCTTCTCAAATTTTAGCATTATAACAACAGCTCTTCTATT CAGGATAGTGCTGAA
GAGGCGTCTAAACTGGATCCAGTGGGCTTCCCTCCTGACTTATTTTTGTCTATTGTGGCCT
TGACTGCCGGGACTAAACTTTACAGCACAACTTGGCAGGACGTGGATTTCATCAGCATGCC
TTTTTCAGCCCTTCCAATTCCTGCCTTCTTTTCAGAAAGTGAGTGTCCAGAAAAGACAATTG
TACAGCAAAGGAATGGACTTTTCTGAAGCTAAATGGAA CACCACAGCCAGAGTTTTCAGTC
ACATCCGTCCTTGGCATGGGCCATGTTCTTATTATAGTCCAGTGTTTTATTCTTCAATGGCT
AATATCTATAATGAAAAGATACTGAAGGAGGGGAACCAGCTCACTGAAAGCATCTTCATACA
GAACAGCAAAC TCTATTTCTTGGCATTCTGTTTAATGGGCTGACTCTGGGCCTTCAGAGGA
GTAACCGTGATCAGATTAAGAACTGTGGATTTTTTATGGCCACAGTGCA TTTTCAGTAGCC
CTTATTTTTGTAACTGCATTCCAGGGCCTTTCAGTGGCTTTCATTCTGAAGTTCCTGGATAA
CATGTTCCATGTCTTGATGGCC CAGGTTACCACTGTCA TTTATCACAACAGTGCTGTCTCTGG
TCTTTGACTTCAGGCCCTCCCTGGAA TTTTCTTGGAAAGCCCATCAGTCCCTTCTCTCTATA
TTTATTTATAATGCCAGCAAGCCCTCAAGTTC CGGAATACGCACCTAGGCAAGAAAGGATCCG
AGATCTAAGTGGCAATCTTTGGGAGCGTTCAGTGGGGATGGAGAAGAACTAGAAAAGACTTA
CCAAACCC AAGAGTGATGAGTCAGATGAAGATACTTTCTAACTGGTACCCACATAGTTTGCA
GCTCTCTTGAACCTTATTTTCACATTTTCAGTGT TTTGTAATATTTATCTTTTCAC TTTTGATA
AACCAGAAATGTTTCTAAATCCTAATATTCTTTG CATATATCTAGCTACTCCCTAAGAGTAA
CCATCCAAGGCTTAGAGTACCCAAAGGCTAAGAAAT TCTAAAGAACTGATACAGAGTAACA
ATATGAAGAATTCA TTAATATCTCAGTACTTGATAAATCAGAAAGTTATATGTGCAGATTAT
TTTCCTTGGCCTTCAAGCTTCCAAAAA ACTTGTAATAATCATGTTAGCTATAGCTTGTATAT
ACACATAGAGATCAATTTGCCAAATATT CACAATCATGTAGTTCTAGTTTACATGCCAAAGT
CTTCCCTTTTTA ACATTATAAAAGCTAGGTTGTCTCTTGAATTTTGAGGCCCTAGAGATAGT
CATTTTGCAAGTAAAGAGCAACGGGACCCTTTCTAAAAACGTTGGTTGAAGGACCTAAATAC
CTGGCCATACCATAGATT TGGGATGATGTAGTCTGTGCTAAATATTTTGCTGAAGAAGCAGT
TTCTCAGACACAACATCTCAGAATTTTAATTTTTAGAAAATTCATGGGAAATTGGATTTTTGT
AATAATCTTTTGATGTTTTAAACATTGGTTCCCTAGTCACCATAGTTACC ACTTGTATTTTA
AGTCATTTAAACAAGCCACGGTGGGGCTTTTTTCTCCTCAGTTTGAGGAGAAAAATCTTGAT
GTCATTACTCCTGAATTATTACATTTTGGAGAATAAGAGGGCATTTTATTTTATTAGTTACT
AATTCAAGCTGTGACTATTGTATATCTTTCCAAGAGTTGAAATGCTGGCTTCAGAATCATAC
CAGATTGT CAGTGAAGCTGATGCCTAGGAACTTTTAAAGGGATCCTTTCAAAGGATCACTT
AGCAAACACATGTTGACTTTTAACTGATGTATGAATATTAATACTCTAAAAATAGAAAGACC
AGTAATATATAAGTCACTTTACAGTGCTACTT CACACTTAAAAGTGCATGGTATTTTTTCATG
GTATTTTGCATGCAGCCAGTTAACTCTCGTAGATAGAGAAGTCAGGTGATAGATGATATTAA
AAATTAGCAAACAAAAGTGACTTGCTCAGGGTCATGCAGCTGGGTGATGATAGAAGAGTGGG
CTTTAACTGGCAGGCCTGTATGTTTACAGACTACCATACTGTAAATATGAGCTTTATGGTGT
CATTTCTAGAACTTATACATTTCTGCTCTCCTTTCTCCTAAGTTTCATGCAGATGAATATA
AGGTAATATACTATTATATAATTCATTTGTGATATCCACAATAATATGACTGGCAAGAATTG
GTGGAAATTTGTAATTAAAATAATTATTAAACCT

FIGURE 9

MEKQCCSHPVICSLSTMYTFLLGAIFIALSSSRILLVKYSANEENKYDYLPTTVNVCSELVK
LVFCVLVSFCVIKKDHQSRNLKYASWKEFSDFMKWSIPAFLYFLDNLI VFYVLSYLQPAMAV
IFS NFSI ITTALLFRIVLKRRLNWIQWASLLTLFLSIVALTAGTKTLQHNLAGRGFHHDAFF
SPSNSCLLFRSECPRKDNCTAKEWTFPEAKWNTTARVFSHIRLGMGHVLIIVQCFISSMANI
YNEKILKEGNQLTESIFIQNSKLYFFGILFNGLTLGLQRSNRDQIKNCGFFYGHSAFSVALI
FVTAFQGLSVAFILKFLDNMFHVLMAQVTTVIITTVSVLVFDFRPSLEFFLEAPSVLLSIFI
YNASKPQVPEYAPRQERIRDL SGNLWERSSSGDGEELERLT KPKSDESEDTF

FIGURE 10

CGTGCCTGCGCAATGGGTGTCGGGTCCGCTTTTTCCCAATCCGGACGTAATCGTGGTTTTTG
TTCTGCAATAGGCGGCTTAGAGGGAGGGGCTTTTTCGCCTATACCTACTGTAGCTTCTCCAC
GTATGGACCCCTAAAGGCTACTGCTGCTACTACGGGGCTAGACAGTTACTGTCTCAGCTCTAG
GATGTGCGTTCTTCCACTAGAAGCTCTTCTGAGGGAGGTAATTAAAAACAGTGGAATGGAA
AAACAGTGCTGTAGTCATCCTGTAATATGCTCCTTGTCAACAATGTATACATTCCTGCTAGG
TGCCATATTCATTGCTTTAAGCTCAAGTCGCATCTTACTAGTGAAGTATTCTGCCAATGAAG
AAAACAAGTATGATTATCTTCCAACACTGTGAATGTGTGCTCAGAACTGGTGAAGCTAGTT
TTCTGTGTGCTTGTGTCATTCTGTGTTATAAAGAAAGATCATCAAAGTAGAAATTTGAAATA
TGCTTCCTGGAAGGAATTCTCTGATTTTCATGAAGTGGTCCATTCCTGCCTTTCTTTATTTCC
TGGATAACTTGATTGTCTTCTATGTCCTGTCCTATCTTCAACCAGCCATGGCTGTTATCTTC
TCAAATTTTAGCATTATAACAACAGCTCTTCTATTTCAGGATAGTGCTGAAGAGGCGTCTAAA
CTGGATCCAGTGGGCTTCCCTCCTGACTTTATTTTTGTCTATTGTGGCCTTGAAGTCCCGGA
CTAAACTTTA

FIGURE 11

CGGACGCGTGGGCGGACGCGTGGGCGGACGCGTGGGGCCGGCTTGGCTAGCGCGGGCGGCC
GTGGCTAAGGCTGCTACGAAGCGAGCTTGGGAGGAGCAGCGGCCTGCGGGGCAGAGGAGCAT
CCCGTCTACCAGGTCCCAAGCGGCGTGGCCCGCGGGTCATGGCCAAAGGAGAAGGCGCCGAG
AGCGGCTCCGCGGCGGGGCTGCTACCCACCAGCATCCTCCAAAGCACTGAACGCCCCGGCCCA
GGTGAAGAAAGAACCGAAAAAGAAGAAACAACAGTTGTCTGTTGCAACAAGCTTTGCTATG
CACTTGGGGGAGCCCCCTACCAGGTGACGGGCTGTGCCCTGGGTTTCTTCCTTCAGATCTAC
CTATTGGATGTGGCTCAGGTGGGCCCTTTCTCTGCCTCCATCATCCTGTTTGTGGGCCGAGC
CTGGGATGCCATCACAGACCCCTGGTGGGCCTCTGCATCAGCAAATCCCCCTGGACCTGCC
TGGGTGCGCTTATGCCCTGGATCATCTTCTCCACGCCCCCTGGCCGTCAATTGCCTACTTCCTC
ATCTGGTTTCGTGCCCCGACTTCCCACACGGCCAGACCTATTGGTACCTGCTTTTCTATTGCCT
CTTTGAAACAATGGTCACGTGTTTCCATGTTCCCTACTCGGCTCTCACCATGTTTCATCAGCA
ACCGAGCAGACTGAGCGGGATTCTGCCACCGCCTATCGGATGACTGTGGAAGTGCTGGGCAC
AGTGCTGGGCACGGCGATCCAGGGACAAATCGTGGGCCAAGCAGACACGCCTTGTTTCCAGG
ACTTCAATAGCTCTACAGTAGCTTCACAAAGTGCCAACCATAACATGGCACCCTTCACAC
AGGGAAACGCAAAAGGCATACCTGCTGGCAGCGGGGTCAATTGTCTGTATCTATATAATCTG
TGCTGTCTATCCTGATCCTGGGCGTGCGGGAGCAGAGAGAACCCTATGAAGCCCAGCAGTCTG
AGCCAATCGCCTACTTCCGGGGCCTACGGCTGGTCACTGAGCCACGGCCCATAACATCAAACCT
ATTACTGGCTTCCTCTTACCTCCTTGGCTTTCATGCTGGTGGAGGGGAACCTTGTCTTGTT
TTGCACCTACACCTTGGGCTTCCGCAATGAATTCCAGAATCTACTCCTGGCCATCATGCTCT
CGGCCACTTTAACCATTCCCATCTGGCAGTGCTTCTTGACCCGGTTTGGCAAGAAGACAGCT
GTATATGTTGGGATCTCATCAGCAGTGCCATTTCTCATCTTGGTGGCCCTCATGGAGAGTAA
CCTCATCATTACATATGCGGTAGCTGTGGCAGCTGGCATCAGTGTGGCAGCTGCCTTCTTAC
TACCCTGGTCCATGCTGCCTGATGTCAATTGACGACTTCCATCTGAAGCAGCCCCACTTCCAT
GGAACCGAGCCCATCTTCTTCTCCTTCTATGTCTTCTTACCAAGTTTGCTCTGGAGTGTC
ACTGGGCATTTCTACCCCTCAGTCTGGACTTTCAGGGTACCAGACCCGTGGCTGCTCGCAGC
CGGAACGTGTCAAGTTTACACTGAACATGCTCGTGACCATGGCTCCCATAGTTCTCATCCTG
CTGGGCCTGCTGCTCTTCAAATGTACCCCATTGATGAGGAGAGGCGGCGGCAGAATAAGAA
GGCCCTGCAGGCACTGAGGGACGAGGCCAGCAGCTCTGGCTGCTCAGAAACAGACTCCACAG
AGCTGGCTAGCATCCTCTAGGGCCCGCCACGTTGCCCCGAAGCCACCATGCAGAAGGCCACAG
AAGGGATCAGGACCTGTCTGCCGGCTTGCTGAGCAGCTGGACTGCAGGTGCTAGGAAGGGAA
CTGAAGACTCAAGGAGGTGGCCCAGGACACTTGCTGTGCTCACTGTGGGGCCGGCTGCTCTG
TGGCCTCCTGCCTCCCCCTCTGCCTGCCTGTGGGGCCAAGCCCTGGGGCTGCCACTGTGAATA
TGCCAAGGACTGATCGGGCCTAGCCCGGAACACTAATGTAGAAACCTTTTTTTTACAGAGCC
TAATTAATAACTTAATGACTGTGTACATAGCAATGTGTGTGTATGTATATGTCTGTGAGCTA
TTAATGTTATTAAATTTTCATAAAAGCTGGAAAGC

FIGURE 12

MWLRWALS LPPSSCLWAEPGMPSQTPWWASA'SANPPGPAWVALCPGSSSPRPWPSLPTSSSG
SCPTSHTARPIGTCFSIASLKQWSRVSMFPTRLSPCSSATEQTERDSATAYRMTVEVLGTVL
GTAIQQQIVGQADTPCFQDFNSSTVASQSANHTHGTTSHRETQKAYLLAAGVIVCIYIICAV
ILILGVREQREPYEAQQSEPIAYFRGLRLVMSHGPYIKLITGFLFTSLAFMLVEGNFVLFCT
YTLGFRNEFQNL LLAIMLSATLTIPWQWFLTRFGKKTAVYVGISSAVPFLILVALMESNLI
ITYAVAVAAGISVAAAFLLPWSMLPDVIDDFHLKQPHFHGTEPIFFSFYVFFTKFASGVSLG
ISTLSLDFAGYQTRGCSQPERVKFTLNMLVTMAPIVLILLGLLLFKMYPIDEERRRQNKAL
QALRDEASSSGCSETDSTELASIL

FIGURE 13

GGGAAACGCAAAGGCATACCTGCTGGCAGCGGGGGTCATTGTCTGTATCTATATAATCTGT
GCTGTCATCCTGATCCTGGGCGTGCGGGAGCAGAGAGAACCCTATGAAGCCCAGCAGTCTGA
GCCAATCGCCTACTTCCGGGGCCTACGGCTGGTCATGAGCCACGGCCCATACATCAAACCTTA
TTACTGGCTTCCTCTTCACCTCCTTGGCTTTTCATGCTGGTGGAGGGGAACCTTGTCTTGTTT
TGCACCTACACCTTGGGCTTCCGCAATGAATTCCAGAATCTACTCCTGGCCATCATGCTCTC
GGCCACTTTAACCATTCCCATCTGGCAGTGGTTCTTGACCCGGTTTGGCAAGAAGACAGCTG
TATATGTTGGGATCTCATCAGCAGTGCCATTTCTCATCTTGGTGGCCCTCATGGAGAGTAAC
CTCATCATTACATATGCGGTAGCTGTGGCAGCTGGCATCAGTGTGGCAGCTGCCTTCTTACT
ACCCTGGTCCATGCTGCCTGATGTCATTGACGACTTCCATCTGAAGCAGCCCCACTTCCATG
GAACCGAGCCCAT

FIGURE 14

GGGGCTTCGGCGCCAGCGGCCAGCGCTAGTCGGTCTGGTAAGGATTTACAAAAGGTGCAGGT
ATGAGCAGGTCTGAAGACTAACATTTTGTGAAGTTGTAAAACAGAAAACCTGTTAGAAATGT
GGTGGTTTCAGCAAGGCCTCAGTTTCCTTCCTTCAGCCCTTGTAATTTGGACATCTGCTGCT
TTCATATTTTCATACATTACTGCAGTAACACTCCACCATATAGACCCGGCTTTACCTTATAT
CAGTGACACTGGTACAGTAGCTCCAGAAAAATGCTTATTTGGGGCAATGCTAAATATTGCGG
CAGTTTTATGCATTGCTACCATTTATGTTTCGTTATAAGCAAGTTCATGCTCTGAGTCCTGAA
GAGAACGTTATCATCAAATTAAACAAGGCTGGCCTTGTAAGTGAATACTGAGTTGTTTAGG
ACTTCTATTGTGGCAAACCTCCAGAAAAACAACCCTTTTGTCTGCACATGTAAGTGGAGCTG
TGCTTACCTTTGGTATGGGCTCATTATATATGTTTGTTCAGACCATCCTTTCCTACCAAATG
CAGCCCCAAATCCATGGCAAACAAGTCTTCTGGATCAGACTGTTGTTGGTTATCTGGTGTGG
AGTAAGTGCACTTAGCATGCTGACTTGCTCATCAGTTTTGCACAGTGGCAATTTTGGGACTG
ATTTAGAACAGAACTCCATTGGAACCCCGAGGACAAAGGTTATGTGCTTCACATGATCACT
ACTGCAGCAGAATGGTCTATGTCATTTTCCTTCTTTGGTTTTTCTGACTTACATTTCGTGA
TTTTCAGAAAATTTCTTTACGGGTGGAAGCCAATTTACATGGATTAACCCCTCTATGACACTG
CACCTTGCCCTATTAACAATGAACGAACACGGCTACTTTCAGAGATATTTGATGAAAGGAT
AAAATATTTCTGTAATGATTATGATTCTCAGGGATTGGGGAAAGGTTACAGAAAGTTGCTTA
TTCTTCTCTGAAATTTTCAACCACTTAATCAAGGCTGACAGTAACACTGATGAATGCTGATA
ATCAGGAAACATGAAAGAAGCCATTTGATAGATTATTCTAAAGGATATCATCAAGAAGACTA
TTAAAAACACCTATGCCTATACTTTTTTATCTCAGAAAATAAAGTCAAAAGACTATG

FIGURE 15

NWWFQQGLSFLPSALVIWTSAAFIYSYITAVTLHHIDPALPYISDTGTVAPEKCLFGAMLNI
AAVLCIATIIYVRYKQVHALSPEENVIIKLNKAGLVLGILSCLGLSIVANFQKTTLFAAHVSG
AVLTFGMGSLYMFVQTILSYQMOPKIHGKQVFWIRLLLVIWCGVSALSMLTCSSVLHSGNFG
TDLEQKLHWNPEDKGYVLHMITTAAEWSMSFSFFGFFLTYYIRDFQKISLRVEANLHGLTLYD
TAPCPINNERTRLLSRDI

FIGURE 16

CGGACGCTTGGGCNGCGCCAGCGGCCAGCGCTAGTCGGTCTGGTAAGTGCCCTGATGCCGAGT
TCCGTCTCTCGGGTCTTTTCCTGGTCCCAGGCAAAGCGGAGCGGAGATCCTCAAACGGCCTA
GTGCTTCGCGCTTCCGGAGAAAATCAGCGGTCTAATTAATTCCTCTGGTTTGTTGAAGCAGT
TACCAAGAATCTTCAACCCTTTCCACAAAAGCTAATTGAGTACACGTTCCCTGTTGAGTACA
CGTTCCTGTTGATTTACAAAAGGTGCAGGTATGAGCAGGTCTGAAGACTAACATTTTGTGAA
GTTGTAAAAACAGAAAACCTGTTAGAAATGTGGTGGTTTCAGCAAGGCCTCAGTTTCCTTCCT
TCAGCCCTTGTAATTTGGACATCTGCTGCTTTTCATATTTTCATACATTACTGCAGTAACACT
CCACCATATAGACCCGGCTTTACCTTATATCAGTGACACTGGTACAGTANC

FIGURE 17

CCCACGCGTCCGCCCCGCGCTGCGTCCCGGAGTGCAAGTGAGCTTCTCGGCTGCCCCGCGGG
CCGGGGTGCGGAGCCGACATGCGCCCCGCTTCTCGGCCTCCTTCTGGTCTTCGCCGGCTGCAC
CTTCGCCTTGTACTTGCTGTGACGCGACTGCCCCGCGGGCGGAGACTGGGCTCCACCGAGG
AGGCTGGAGGCAGGTGCTGTGGTTCCCCTCCGACCTGGCAGAGCTGCGGGAGCTCTCTGAG
GTCCTTCGAGAGTACCGGAAGGAGCACAGGCCTACGTGTTCTGCTCTTCTGCGGCGCCTA
CCTCTACAAACAGGGCTTTGCCATCCCCGGCTCCAGCTTCTGAATGTTTTAGCTGGTGCCT
TGTTTGGGCCATGGCTGGGGCTTCTGCTGTGCTGTGTTGACCTCGGTGGGTGCCACATGC
TGCTACCTGCTCTCCAGTATTTTTGGCAAACAGTTGGTGGTGTCTACTTTCTGATAAAGT
GGCCCTGCTGCAGAGAAAGGTGGAGGAGAAAGAAACAGCTTGTTTTTTTTCTTATTGTTTT
TGAGACTTTTTCCCATGACACCAAAGTGGTTCTTGAACCTCTCGGCCCCAATTCTGAACATT
CCCATCGTGCAGTTCTTCTTCTCAGTTCTTATCGGTTTGATCCCATATAATTTTCATCTGTGT
GCAGACAGGGTCCATCCTGTCAACCCTAACCTCTCTGGATGCTCTTTTCTCCTGGGACACTG
TCTTTAAGCTGTTGGCCATTGCCATGGTGGCATTAAATCCTGGAACCCTCATTAAAAAATTT
AGTCAGAAACATCTGCAATTGAATGAAACAAGTACTGCTAATCATATACAGTAGAAAAGA
CACATGATCTGGATTTTCTGTTTGCCACATCCCTGGACTCAGTTGCTTATTTGTGTAATGGA
TGTGGTCTCTAAAGCCCCCTCATTGTTTTTGATTGCCTTCTATAGGTGATGTGGACACTGTG
CATCAATGTGCAGTGTCTTTTCAGAAAGGACACTCTGCTCTTGAAGGTGTATTACATCAGGT
TTTCAAACCAGCCCTGGTGTAGCAGACACTGCAACAGATGCCTCCTAGAAAATGCTGTTTGT
GGCCGGGCGCGGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCCGGTGATT
ACAAGGTCAGGAGTTCAAGACCAGCCTGGCCAAGATGGTGAAATCCTGTCTCTAATAAAAAT
ACAAAAATTAGCCAGGCGTGGTGGCAGGCACCTGTAATCCCAGCTACTCGGGAGGCTGAGGC
AGGAGAATTGCTTGAACCAAGGTGGCAGAGGTTGCAGTAAGCCAAGATCACACCACTGCACT
CCAGCCTGGGTGATAGAGTGAGACACTGTCTTGAC

FIGURE 18

MRPLLGLLLVFAGCTFALYLLSTRLPRGRRLGSTEEAGGRSLWFPSDLAELRELSEVLREYR
KEHQAYVFLFLFCGAYLYKQGFAIPGSSFLNVLAGALFGPWLGLLLCCVLTSVGATCCYLLSS
IFGQLVVSYPDKVALLQRKVEENRNSLFFLLFLRLFPMTPNWFLNLSAPILNIPIVQFF
FSVLIGLIPYNFICVQTGSILSTLTSLDALFSWDTVFKLLAIAMVALIPGTLIKKFSQKHLQ
LNETSTANHIHSRKDT

FIGURE 19

CCGAGGCGGGAGGAGCCCGAGGGGGCGCGAGCCCCGCATGAATCATTGTAGTCAATCATT
CCAGTTCTCAGCCGCTCAGTTGTGATCAAGGGACACGTGGTTTCCGAACTGCCAGCTCAGAA
TAGGAAAATAACTTGGGATTTTATATTGGAAGACATGGATCTTGCTGCCAACGAGATCAGCA
TTTATGACAACTTTTCTCAGAGACTGTTGATTGGTGAGACAGACCGGCCATCAGTGTGGCATG
TCAGAGAAGGCAATTGAAAAATTTATCAGACAGCTGCTGGAAAAGAATGAACCTCAGAGACC
CCCCCGCAGTATCCTCTCCTTATAGTTGTGTATAAGGTTCTCGCAACCTTGGGATTAATCT
TGCTCACTGCCTACTTTGTGATTCAACCTTTTCTCAGCCCATTAGCACCTGAGCCAGTGTCTTCT
GGAGCTCACACCTGGCGCTCACTCATCCATCACATTAGGCTGATGTCCTTGCCCATTGCCAA
GAAGTACATGTGAGAAAATAAGGGAGTTCCTCTGCATGGGGGTGATGAAGACAGACCCCTTCT
CAGACTTTGACCCCTGGTGGACAAACGACTGTGAGCAGAATGAGTCAGAGCCCATTCTGCCC
AACTGCACTGGCTGTGCCCAGAAACACCTGAAGGTGATGCTCCTGGAAGACGCCCCAAGGAA
ATTTGAGAGGCTCCATCCACTGGTGATCAAGACGGGAAAGCCCCTGTTGGAGGAAGAGATTC
AGCATTTTTTGTGCCAGTACCCTGAGGCGACAGAAGGCTTCTCTGAAGGGTTTTTCGCCAAG
TGGTGGCGCTGCTTTCTGAGCGGTGGTTCCCATTTCTTATCCATGGAGGAGACCTCTGAA
CAGATCACAAATGTTACGTGAGCTTTTTCTGTTTTCACTCACCTGCCATTTCCAAAAGATG
CCTCTTTAAACAAGTGCTCCTTTCTTCACCCAGAACCTGTTGTGGGGAGTAAGATGCATAAG
ATGCCTGACCTATTTATCATTGGCAGCGGTGAGGCCATGTTGCAGCTCATCCCTCCCTTCCA
GTGCCGAAGACATTGTCTGCTGTGGCCATGCCAATAGAGCCAGGGGATATCGGCTATGTGCG
ACACCACCCACTGGAAGGTCTACGTTATAGCCAGAGGGGTCCAGCCTTTGGTCATCTGCGAT
GGAACCGCTTTCTCAGAACTGTAGGAAATAGAACTGTGCACAGGAACAGCTTCCAGAGCCGA
AAACCAGGTTGAAAGGGGAAAAATAAAAACAAAACGATGAACTGCAAAAA

FIGURE 20

MDLAANEISIIYDKLSETVDLVRQTGHQCGMSEKAIEKFIRQLLEKNEPQRPPQYPLLIVVY
KVLATLGLILLTAYFVIQPFSPPLAPEPVLGAHTWRSLIHHIRLMSLP IAKKYMSENKGVPL
HGGDEDRPFPDFDPWWTNDCEQNESEPI PANCTGCAQKHLKVMLLEDAPRKFERLHPLVIKT
GKPLLEEEIQHFLCQYPEATEGFSEGFFAKWWRCFPERWFPPYPWRRPLNRSQMLRELFV
FTHLPFPKASLNKCSFLHPEPVVGSKMHKMPDLFIIGSGEAMLQLIPPFQCRRCQSVAMP
IEPGDIGYVDTTHWKVYVIARGVQPLVICDGTAFSEL

FIGURE 21

CCACGGTGTCCGTTCTTCGCCCCGGCGGCAGCTGTCCCCGAGGCGGGAGGAGCCCCGAGGGGCG
CGAGCCCCGCATGAATCATTGTAGTCAATCATTTTCCAGTTCTCAGCCGTTTCAGTTGTGATC
AAGGGACACGTGGTTTCCGAAC TGCCAGCTCAGAATAGGAAAATAACTTGGGATTTTATATT
GGAAGACATGGATCTTGCTGCCAACGAGATCAGCATTTATGACAACTTTTCAGAGACTGTTG
ATTTGGTGAGACAGACCGGCCATCAGTGTGGCATGT CAGAGAAGGCAATTGAAAAATTTATC
AGACAGCTGCTGGAAAAGAATGAACCTCAGAGACCCCCCGCAGTATCCTCTCCTTATAGT
TGTGTATAAGGTTCTCGCAACCTTGGGATTAATCTTGCTCACTGCCTACTTTGTGATTCAAC
CTTTCAGCCCATTAGCACCTGAGCCAGTGCTTTGTGGAGCTCAC

FIGURE 22

CCCACGCGTCCGCCCCACGCGTCCGGCTGAACACCTCTTCTTTGGAGTCAGCCACTGATGAGG
 CAGGGTCCCCAATTGACAGCTGCAGCAGCTGCAGCAGCTGCAGAGCGCTGCTCCTGGCTGGTG
 CCACTGGTGCGCACGCTGCTAGACCGTGCCCTATGAGCCGCTGGGGCTGCAGTGGGGACTGCC
 CTCCCTGCCACCCACCAATGGCAGCCCCACCTTCTTTGAAGACTTCCAGGCTTTTTGTGCCA
 CACCCGAATGGCGCCACTTCATCGACAAACAGGTACAGCCAACCATGTCCCAGTTCGAAATG
 GACACGTATGCTAAGAGCCACGACCTTATGTGAGGTTTCTGGAATGCCTGCTATGACATGCT
 TATGAGCAGTGGGCAGCGGCGCCAGTGGGAGCGCGCCAGAGTCGTGGGGCCTTCCAGGAGC
 TGGTGCTGGAACCTGCGCAGAGGCGGGCGCGCTGGAGGGGCTACGCTACACGGCAGTGCTG
 AAGCAGCAGGCAACGCAGCACTCCATGGCCCTGCTGCACTGGGGGGCGCTGTGGCGCCAGCT
 CGCCAGCCCATGTGGGGCCTGGGCGCTGAGGGACACTCCCATCCCCGCTGGAAACTGTCCA
 GCGCCGAGACATATTACGCATGCGTCTGAAGCTGGTGCCCAACCATCACTTCGACCCTCAC
 CTGGAAGCCAGCGCTCTCCGAGACAATCTGGGTGAGGTTCCCCTGACACCCACCGAGGAGGC
 CTCCTGCTCTGGCAGTGACCAAGAGGCCAAAGTGAGCACCCACCCAGATTGCTGCAGG
 AGGACCAGCTCGGCGAGGACGAGCTGGCTGAGCTGGAGACCCGATGGAGGCAGCAGAATG
 GTGAGCAGCGTGAGAAGCTGGTGCTGTGCGCCGAGTGCCAGCTGGTGACGGTAGTGCCGT
 GGTCCCAGGGCTGCTGGAGGTCAACACAGAAATGTATACTTCTACGATGGCAGCACTGAGC
 GCGTGGAACCGAGGAGGGCATCGGCTATGATTTCCGGCGCCCACTGGCCAGCTGCGTGAG
 GTCCACCTGCGGCGTTTCAACCTGCGCCGTTGAGCACTTGAGCTCTTCTTTATCGATCAGGC
 CAACTACTTCTCAACTTCCCATGCAAGTGCGGCACGACCCAGTCTCATCTCCTAGCCAGA
 CTCGAGACCCACGCTGGCCCCATCCCCACCCCATACCCAGGTACGGAACCAGGTGTACTCG
 TGGCTCCTGCGCCTACGGCCCCCTCTCAAGGCTACCTAAGCAGCCGCTCCCCCAGGAGAT
 GCTGCGTGCTCAGGCCTTACCCAGAAATGGGTACAGCGTGAGATATCCAACCTTCGAGTACT
 TGATGCAACTCAACACCATTGCGGGGCGGACCTACAATGACCTGTCTCAGTACCCTGTGTTT
 CCCTGGGTCTTGACGAGTACGTGTCCCCAACCCCTGGACCTCAGCAACCCAGCCGCTTCCG
 GGACCTGTCTAAGCCCATCGGTGTGGTGAACCCCAAGCATGCCAGCTCGTGAGGGAGAAGT
 ATGAAAGCTTTGAGGACCAGCAGGGACCATTGACAAGTTCCACTATGGCACCCACTACTCC
 AATGCAGCAGGCGTGATGCACTACCTCATCCGCGTGAGCCCTTCACTCCCTGCACGTCCA
 GCTGCAAAGTGCGCGCTTTGACTGCTCCGACCGGCACTTCCACTCGGTGGCGGCAGCTGGC
 AGGCACGCTGGAGAGCCCTGCCGATGTGAAGGAGCTCATCCCGGAATTCTTCTACTTTCT
 GACTTCTGGAGAACCAGAACGGTTTTGACCTGGGCTGTCTCCAGCTGACCAACGAGAAGGT
 AGGCGATGTGGTGCTACCCCGTGCGCCAGCTCTCCTGAGGACTTCATCCAGCAGCACCGCC
 AGGCTCTGGAGTCGGAGTATGTGTCTGCACACCTACACGAGTGGATCGACCTCATCTTTGGC
 TACAAGCAGCGGGGGCCAGCCGCGGAGGAGCCCTCAATGTCTTCTATTACTGCACCTATGA
 GGGGCTGTAGACCTGGACCATGTGACAGATGAGCGGGAACGGAAGGCTCTGGAGGGCATT
 TCAGCAACTTTGGGCAGACTCCCTGTGAGCTGTGAAGGAGCCACATCCAACCTCGGCTCTCA
 GCTGAGGAAGCAGCCCATCGCCTTGACGCGCTGGACACTAATCACTACCTAGCATCTTCCAGCA
 CCTGGACGAACTCAAGGCATTCTTCGAGAGGTGACTGTGAGTGCCAGTGGGCTGCTGGGCA
 CCCACAGCTGGTTGCCCTATGACCGCAACATAAGCAACTACTTCAGCTTCAGCAAGAACCC
 ACCATGGGCAGCCACAAAGACGCAGCGACTGCTGAGTGGCCCGTGGGTGCCAGGCAGTGGTGT
 GAGTGGACAAGCACTGGCAGTGGCCCCGATGGAAAGCTGCTATTAGCGGTGGCCACTGGG
 ATGGCAGCCTGCGGGTGACTGCACTACCCCGTGGCAAGCTGTTGAGCCAGCTCAGTGCCAC
 CTTGATGTAGTAACCTGCCTTGCACTGGACACCTGTGGCATCTACCTCATCTCAGGCTCCCG
 GGACACCACGTGCATGGTGTGGCGGCTCCTGCATCAGGGTGGTCTGTGAGTAGGCTGGCAC
 CAAAGCCTGTGACAGTCTGTATGGGCATGGGGCTGCAGTGAGCTGTGTGGCCATCAGCACT
 GAACTTGACATGGCTGTGTCTGGATCTGAGGATGGAAGTGTGATCATACACACTGTACGCCG
 CGGACAGTTTGTAGCGGCACTACGGCTCTGGGTGCCACATTCCCTGGACCTATTTTCCACC
 TGGCATTGGGGTCCGAAGGCCAGATTGTGGTACAGAGCTCAGCGTGGGAACGTCTTGGGGCC
 CAGGTACCTACTCCTTGACCTGTATTCACTCAATGGGAAGTTGCGGGCTTCACTGCCCTT
 GGCAGAGCAGCCTACAGCCCTGACGGTGACAGAGGACTTTGTGTTGCTGGGCACCGCCAGT
 GCGCCCTGCACATCCTCCAACATAACACTGCTCCCGGCCGCGCCTCCCTTGCCCATGAAG
 GTGGCCATCCGCAGCGTGCGCGTGACCAAGGAGCGCAGCCACGTGCTGGTGGGCTGGAGGA
 TGGCAAGCTCATCGTGGTGGTCCGCGGCGCAGCCCTCTGAGGTGCGCAGCAGCGTTCGCGC
 GGAAGCTGTGGCGTCTCGCGCGCATCTCCAGGTGTCTCGGGAGAGACGGAATAACAAC
 CTACTGAGGCGCGCTGAACCTGGCCAGTCCGGCTGCTCGGGCCCCGCCCCGGCAGGCCTG
 GCCGGGAGGCCCGCCAGAAAGTCGGCGGGAACACCCCGGGGTGGGCGAGCCAGGGGGTGA
 GCGGGGCCACCTGCCAGCTCAGGGATTGGCGGGCGATGTTACCCCTCAGGGATTGGCG
 GCGGAAGTCCCGCCCTCGCCGGCTGAGGGGCCGCTGAGGGCCAGCACTGGCGTCT

FIGURE 23

MSQFEMDTYAKSHDLMSGFWNACYDMLMSSGQRRQWERAQSRRAFQELVLEPAQRRARLEGL
RYTAVLKQQATQHSMALLHWGALWRQLASPCGAWALRDTPIPRWKLSSAETYSRMRLKLVPN
HHFDPHLEASALRDNLGEVPLTPTEEASLPLAVTKEAKVSTPPELLQEDQLGEDELAELTP
MEAAELDEQREKLVLSAECQLVTVVAVVPGLLEVTTQNVYFYDGSTERVETEEGIGYDFRRP
LAQLREVHLRRFNLRRSALELFFIDQANYFLNFPCKVGTPVSSPSQTPRPQPGPIPPHTQV
RNQVYSWLLRLRPPSQGYLSSRSPQEMLRASGLTQKWVQREISNFEYLMQLNTIAGRITYNDL
SQYPVFPWVLQDYVSPTLDLSNPAVFRDLSKPIGVVNPKHAQLVREKYESFEDPAGTIDKFH
YGTHYSNAAGVMHYLIRVEPFTSLHVQLQSGRFDCSDRQFHSVAAAWQARLESPADVKEIP
EFFYFPDFLENQNGFDLGCLQLTNEKVGDVVLPWASSPEDFIQQHRQALESEYVSAHLHEW
IDLIFGYKQRGPAEEEEALNVFYCYEGAVDLDHVTDERERKALEGIIISNFGQTPCQLLKEP
HPTRLSAEEAAHRLARLDTNPSIFQHLDELKAFFAEVTVSASGLLGTHSWLPYDRNISNYF
SFSKDPTMGSHKTQRLLSGPWVPGSGVSGQALAVAPDGKLLFSGGHWGSLRVTALPRGKLL
SQLSCHLDVVTCLALDTCGIYLSGSRDTCMVWRLLHQGLSVGLAPKPVQVLYGHGAAVS
CVAISTELDMAVSGSEDGTVIHTVRRGQFVAALRPLGATFPGPIFHLALGSEGQIVVQSSA
WERPGAQVTYSLHLYSVNGKLRASLPLAEQPTALTVTEDFVLLGTAQCALHILQLNTLLPAA
PPLPMKVAIRSVAVTKERSHVLVGLEDGKLIVVAGQPSEVRSSQFARKLWRSSRRISQVSS
GETEYNPTAR

FIGURE 24

CGGACGCGTGGGCGGACGCGTGGGGCTGTGAGAAAGTGCCAATAAATACATCATGCAACCC
CACGGCCACCTTGTGAACTCCTCGTGCCAGGGCTGATGTGCGTCTTCCAGGGCTACTCAT
CCAAAGGCCTAATCCAACGTTCTGTCTTCAATCTGCAAATCTATGGGGTCTGGGGCTCTTC
TGGACCCTTAACTGGGTACTGGCCCTGGGCCAATGCGTCCTCGCTGGAGCCTTTGCCTCCTT
CTACTGGGCCTTCCACAAGCCCCAGGACATCCCTACCTTCCCCTTAATCTCTGCCTTCATCC
GCACACTCCGTTACCACACTGGGTCAATTGGCATTGTGGAGCCCTCATCCTGACCCTTGTGCAG
ATAGCCCGGTCATCTTGGAGTATATTGACCACAAGCTCAGAGGAGTGCAGAACCCCTGTAGC
CCGCTGCATCATGTGCTGTTTCAAGTGCTGCCTCTGGTGTCTGGAAAAATTTATCAAGTTCC
TAAACCGCAATGCATACATCATGATCGCCATCTACGGGAAGAATTTCTGTGTCTCAGCCAAA
AATGCGTTCATGCTACTCATGCGAAACATTGTCAGGGTGGTTCGTCTGGACAAAGTCACAGA
CCTGCTGCTGTTCTTTGGGAAGCTGCTGGTGGTTCGGAGGCGTGGGGGTCTGTCTCTTTT
TTTTCTCCGGTCGCATCCCGGGGCTGGGTAAAGACTTTAAGAGCCCCACCTCAACTATTAC
TGGCTGCCCATCATGACCTCCATCCTGGGGGCTATGTTCATCGCCAGCGGCTTCTTCAGCGT
TTTCGGCATGTGTGTGGACACGCTCTTCCTCTGCTTCCTGGAAGACCTGGAGCGGAACAACG
GCTCCCTGGACCGGCCCTACTACATGTCCAAGAGCCTTCTAAAGATTCTGGGCAAGAAGAAC
GAGGCGCCCCCGGACAACAAGAAGAGGAAGAAGTGAAGCAGCTCCGGCCCTGATCCAGGACTGC
ACCCACCCCCACCGTCCAGCCATCCAACCTCACTTCGCCTTACAGGTCTCCATTTTGTGGT
AAAAAAGGTTTTAGGCCAGGCGCCGTGGCTCACGCCTGTAATCCAACACTTTGAGAGGCTG
AGGCGGGCGGATCACCTGAGTCAGGAGTTCGAGACCAGCCTGGCCAACATGGTGAAACCTCC
GTCTCTATTAAAAATACAAAAATTAGCCGAGAGTGGTGGCATGCACCTGTCTATCCAGCTAC
TCGGGAGGCTGAGGCAGGAGAATCGCTTGAACCCGGGAGGCAGAGGTTGCAGTGAGCCGAGA
TCGCGCCACTGCACTCCAACCTGGGTGACAGACTCTGTCTCCAAAACAAAACAAACAA
AAAGATTTTATTAAAGATATTTTGTAACTC

FIGURE 25

RTRGRTRGGCEKVPINTSCNPTAHLVNSSCPGLMCVFQGYSSKGLIQRSVFNLQIYGVLG
LFWTLNWWLALGQCVLAGAFASFYWAFHKPDIPFPLISAFIRTLRYHTGSLAFGALILTLVQ
IARVILEYIDHKLRGVQNPVARCIMCCFKCCLWCLEKFIKFLNRNAYIMIAIYGKNFCVSAK
NAFMLLMRNIVRVVLDKVTDLLFFGKLLVVGGVGVLSFFFFSGRIPGLGKDFKSPHLNYY
WLPIMTSILGAYVIASGFFSVFGMCVDTLFLCFLEDLERNNGSLDRPYMSKSLKILGKKN
EAPPDNKKRKK

FIGURE 26

GAGTCTTGACCGCCGCCGGGCTCTTGGTACCTCAGCGCGAGCGCCAGGCGTCCGGCCGCCGT
GGCTATGTTTCGTGTCCGATTTCCGCAAAGAGTTCTACGAGGTGGTCCAGAGCCAGAGGGTCC
TTCTCTTCGTGGCCTCGGACGTGGATGCTCTGTGTGCGTGCAAGATCCTTCAGGCCTTGTTTC
CAGTGTGACCACGTGCAATATACGCTGGTTCCAGTTTCTGGGTGGCAAGAAGCTTGAAACTGC
ATTTCTTGAGCATAAAGAAGAGTTTCATTATTTTATTCTCATAACTGTGGAGCTAATGTAG
ACCTATTGGATATTCTTCAACCTGATGAAGACACTATATTCTTTGTGTGTGACTCCCATAGG
CCAGTCAATGTTCGTCAATGTATACAACGATACCCAGATCAAATTACTCATTAAACAAGATGA
TGACCTTGAAGTTCCCGCCTATGAAGACATCTTCAGGGATGAAGAGGAGGATGAAGAGCATT
CAGGAAATGACAGTGATGGGTGAGAGCCTTCTGAGAAGCGCACACGGTTAGAAGAGGAGATA
GTGGAGCAAACCATGCGGAGGAGGCAGCGGCGAGAGTGGGAGGCCCGGAGAAGAGACATCCT
CTTTGACTACGAGCAGTATGAATATCATGGGACATCGTCAGCCATGGTGATGTTTGAGCTGG
CTTGATGCTGTCCAAGGACCTGAATGACATGCTGTGGTGGGCCATCGTTGGACTAACAGAC
CAGTGGGTGCAAGACAAGATCACTCAAATGAAATACGTGACTGATGTTGGTGTCTTGCAGCG
CCACGTTTTCCCGCCACAACCACCGGAACGAGGATGAGGAGAACACACTCTCCGTGGACTGCA
CACGGATCTCCTTTGAGTATGACCTCCGCCTGGTGCTCTACCAGCACTGGTCCCTCCATGAC
AGCCTGTGCAACACCAGCTATACCGCAGCCAGGTTCAAGCTGTGGTCTGTGCATGGACAGAA
GCGGCTCCAGGAGTTTCCTTGAGACATGGGTCTTCCCCTGAAGCAGGTGAAGCAGAAGTTCC
AGGCCATGGACATCTCCTTGAAGGAGAATTTGCGGGAAATGATTGAAGAGTCTGCAAATAAA
TTTGGGATGAAGGACATGCGCGTGACAGTCTTCAGCATTCATTTTGGGTTCAAGCACAAGTT
TCTGGCCAGCGACGTGGTCTTTGCCACCATGTCTTTGATGGAGAGCCCCGAGAAGGATGGCT
CAGGGACAGATCACTTCATCCAGGCTCTGGACAGCCTCTCCAGGAGTAACCTGGACAAGCTG
TACCATGGCCTGGAACCTCGCCAAGAAGCAGCTGCGAGCCACCCAGCAGACCATTGCCAGCTGC
CTTTGCACCAACCTCGTCATCTCCAGGGGCTTTTCTGTACTGCTCTCTCATGGAGGGCAC
TCCAGATGTCATGCTGTTCTTAGGCCGGCATCCCTAAGCCTGCTCAGCAAACACCTGCTCA
AGTCCTTTGTGTGTTTCGACAAAGAACCGGCGCTGCAAACCTGCTGCCCCCTGGTGATGGCTGCC
CCCCTGAGCATGGAGCATGGCACAGTGACCGTGGTGGGCATCCCCCAGAGACCGACAGCTC
GGACAGGAAGAACTTTTTTGGGAGGGCGTTTGAGAAGGCAGCGGAAAGCACCAGCTCCCGGA
TGCTGCACAACCATTTTGACCTCTCAGTAATTGAGCTGAAAGCTGAGGATCGGAGCAAGTTT
CTGGACGCACCTTATTTCCCTCCTGTCTTAGGAATTTGATTCTTCCAGAATGACCTTCTTATT
TATGTAACCTGGCTTTCATTTAGATTGTAAGTTATGGACATGATTTGAGATGTAGAAGCCATT
TTTTATTAAATAAAATGCTTATTTTAGGAAA

FIGURE 27

MFVSDFRKEFYEVVQSQRVLLFVASDVDALCACKILQALFQCDHVQYTLVPVSGWQELETAF
LEHKEQFHYFILINCGANVDLLDILQPDEDITFFVCDSHRPVNVNVYNDTQIKLLIKQDDD
LEVPAIEDIFRDEEEDEEHSGNDSGSEPEKTRLEEEIVEQTMRRRQRREWEARRRDILF
DYEQYEHGTSSAMVMFELAWMLSKDLNDMLWWAIVGLTDQWVQDKITQMKYVTDVGVLRH
VSRHNRNEDEENTLSVDCTRISFEYDLRLVLYQHWSLHDSLNTSYTAARFKLWSVHGQKR
LQEFADMGLPLKQVKQKFQAMDISLKENLREMIEESANKFGMKDMRVQTFSIHFGFKHKFL
ASDVVFATMSLMESPEKDGSGTDHFIQALDSLRSNLDKLYHGLELAKKQLRATQQTIASCL
CTNLVISQGPFLYCSLMEGTPDVMLFSRPASLSLLSKHLLKSFVCSTKNRRCKLLPLVMAAP
LSMEHGTVTTVVGIPPETDSSDRKNFFGRAFEKAAESTSSRMLHNHFDLSVIELKAEDRSKFL
DALISLLS

FIGURE 28

GTACCTCAGCGCGAGCGCCAGGGCGTCCGGCCGCGGTGGCTATGNTCGTGTCCGATTTCCGCA
AAGAGTTCTACGAGGTGGTCCAGAGCCAGAGGGTCCTTCTCTTCGTGGCCTCGGANGTGGAT
GCTCTGTGTGCGTGCAAGATCCTTCAGGCCTTGTTCCAGTGTGACCANGTGCAATATANGCT
GGTTCCAGTTTCTGGGTGGCAAGAACTTGAAACTGCATTTCTTGAGCATAAAGAACAGTTTC
ATTATTTTATTCTCATAAACTGTGGAGCTAATGTAGACCTATTGGATATTCTTCAACCTGAT
GAAGACACTATATTCTTTGTGTGTGACACCCATAGGCCAGTCAATGTTGTCAATGTATACAA
CGATACCC

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FIGURE 29

CAGGAACCCCTCTCTTTGGGTCTGGATTGGGACCCCTTTCCAGTACCATTTTTTCTAGTGAAC
CACGAAGGGACGATACCAGAAACACCCCTCAACCCAAAGGAAATAGACTACAGCCCCAATTG
GCTGACTTTTGGCTATAGAA1AAAGAAAGGAACGAAAAGAGACAGTTTTTTTTTGGAAAGCTAA
GTCTTCCCTTTATCGAGTCAAGAAACCCCCCTTCTTGAGCTATTTACAGCTTTTAACAATT
GAGTAAAGTACGCTCCGGTCACCATGGTGACAGCCGCCCTGGGTCCCGTCTGGGCAGCGCTC
CTGCTCTTTCTCCTGATGTGTGAGATCCGTATGGTGGAGCTCACCTTTGACAGAGCTGTGGC
CAGCGGCTGCCAACGGTGCTGTGACTCTGAGGACCCCTGGATCCTGCCCATGTATCCTCAG
CCTCTTCTCCTCCGGCCGCCCCACGCCCTGCCTGAGATCAGACCCTACATTAATATCACCATC
CTGAAGGGTGACAAAGGGGACCCAGGCCCAATGGGCCTGCCAGGGTACATGGGCAGGGAGGG
TCCCAAGGGGAGCCTTGGCCCTCAGGGCAGCAAGGGTGACAAGGGGAGATGGGCAGCCCCG
GCGCCCCGTGCCAGAAGCGCTTCTTCGCCCTTCTCAGTGGGCCGCAAGACGGCCCTGCACAGC
GGCGAGGACTTCCAGACGCTGCTCTTCAAGAGGGTCTTTGTGAACCTTGATGGGTGCTTTGA
CATGGCGACCGGCCAGTTTGCTGCTCCCCCTGCGTGGCATCTACTTCTTCAGCCTCAATGTGC
ACAGCTGGAATTACAAGGAGACGTACGTGCACATTATGCATAACCAGAAAGAGGCTGTCTC
CTGTACGCGCAGCCAGCGAGCGCAGCATCATGCAGAGCCAGAGTGTGATGCTGGACCTGGC
CTACGGGACCGCGTCTGGGTGCGGCTCTTCAAGCGCCAGCGCAGAGAACGCCATCTACAGCA
ACGACTTCGACACCTACATCACCTTCAGCGGCCACCTCATCAAGGCCGAGGACGACTGAGGG
CCTCTGGGCCACCCCTCCCGGCTGGAGAGCTCAGGTGCTGGTCCCGTCCCTGCAGGGCTCAG
TTTGCACTGCTGTGAAGCAGGAAGGCCAGGGAGGTCCCGGGGACCTGGCATCTTGGGGAGA
CCCTGCTTCTATCTTGGCTGCCATCATCCCTCCAGCCTATTTCTGCTCCTCTCTCTCT
TGGACCTATTTTAAGAAGCTTGCTAACCTAAATATTCTAGAACTTTCCAGCCTCGTAGCCC
AGCACTTCTCAAACCTTGGAAATGCATGCCAATCACCCGGGGTTCGTGTTAAATGCAGATTCT
GACTCAGCAGGTCTGAGTGGGTCCAGGATTCTGTGTTTCTCATATGTTCTTGGGTGATGCTG
ATGGGGTCAGTCTATGAACCACACTGGAGCAACCAGGTTCTAGGACTTTCTCAATATTCTAG
TACTTTCTGAACATTCTGGAATCCTCCCCACATTCTAGAATTCTCCCCAACATTTTTTTTTCT
TGAGACAGAGTCTTGCTCTGTTGCCCAGGCTAGAGTGCAGTGGTGCAATCTCAGTTCACCTGC
AACCTCTGCCTCCCGGGTTCAGCGGATTCTTCTGCCTCAGCCTCCCTAGTGGCTGGGATTAC
AGGCGCCTGCTACCATGCCTGGCTAATTTTTGTATTTTTAGTAGAGATGGGGTTTACCATA
TTGGCCAGGCTGGTCTTGAACCTCCTGACTTCAGGTGACCCACCCGCTCGGCCCTCAAAAT
TGCTGGGATTACAGGTGTGAGCCACCGTGCCTGGCCAATTCCAACATTCTTAAATTCTCTCAT
CCCTCCAGGGCTCCCGTGTCTATGTTCTCTTTACCCCTTCCCCCTCTTCTCTTGTCTCAGGCC
TGCACCACTGCAGCCACCGTTCATTATTCATTCAATTAACACTGAGCACTCACTCTGTGCT
GGGTCCCGGGAAGGGTGAGGGGGTCAGACACAGGCCCTGCCCTGCCCTCAGTGAAGTGGCCA
GTCCAGCCAGGCGGGGAGAGATGTGTACATAGGTTTAAAGCAGACCCAGAGCTCATGGGG
GCCTGTGTTCTGGGTGTTTCAAGTGTCTGCTGGTCTCCATTACCCACTGCTCCCCAAGGCTGG
TGGGACGGGTCCCGGTGGCAGGGGCAGGTATCTCCTTCCCGTTCCTCATCCACCTGCCAG
TGCTCATCGTTACAGCAAACCCAGGGGGCCTTGGCCAGGTCAAGGGTCTGTGAGGAGAGG
ACCCAGGAGTGTGGGGCATTTGGGGGGTGAAGTGGCCCCCGAAGAATGGAACCCACACCCA
TAGCTCTCCCCACAGCTGATACGGCATCTTGCAGAGAAGACCTGCCCTCCTCACTGGGATCCC
CTTCTGCTCCTCCCAGGGCTCTGCCAGGGCCTTGCTCAGTCCCTTCCACCAAAGTCATCT
GAACTTCCGTTTCCCCAGGGCCTCCAGCTGCCCTCAGACACTGATGTCTGTCCCCAGGTGCT
CTCTGCCCTCATGCCCCCTCTCACCGGCCAGTGCCCCGACTCTCCAGGCTTTATCAAGGTG
CTAAGGCCCGGGTGGGCAGCTCCTCGTCTCAGAGCCCTCCTCCGGCCTGGTGTGCTTCTTAC
AAACACCTGCAGGAGAAGGGCCACGGAAGCCCAGGCTTTAGAGCCCTCAGCAGGTCTGGGG
AGCTAGAGCAAAGGAGGGACCTCAGGCCTTCCGTTTCTTCTTCCAGGGTGGGGTGGCCTGGT
GTTCCCCCTAGCCTTCCAACCCAGGTGGCCTGCCCTTCTCCCCAGAGGGAGGCGGCTCCGC
CCATTGGTGCTCATGCAGACTCTGGGGCTGAGGTGCCCGGGGGTGATCTCTGGTGCTCAC
AGCCGAGGGAGCCGTGGCTCCATGGCCAGATGACGGAACAGGGTCTGACCAAGTGCCAGGA
AGACCTGTGCTATAAACACCCCTGCCTGATCCTGCCCTGCCTGACCCCGCCACGCCCTGCC
GTCCAGCATGATTAAAGAAATGCTGTCTCCTCTTGAAAAAAAAAAAAAAAAA

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FIGURE 30

MVTAALGPVWAALLLFLLMCEIRMVELTFDRAVASGCQRCCDSEDPLDPAHVSSASSSSGRPH
ALPEIRPYINITILKGDKGDPGPMGLPGYMGREGPQGEPPGPQSGDKGEMGSPGAPCQKRF
FAFSVGRKTALHSGEDFQTLLEFVFNLDGCFDMATGQFAAPLRGIYFFSLNVHSWNYKET
YVHIMHNQKEAVILYAQPSESRIMQSQSVMLDLAYGDRVWVRLFKRQRENAIYSNDFDTYIT
FSGHLIKAEDD

Important features:

Signal peptide:

amino acids 1-20

N-glycosylation site.

amino acids 72-75

Clq domain proteins.

amino acids 144-178, 78-111 and 84-117

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FIGURE 31

ACTCGAACGCAGTTGCTTCGGGACCCAGGACCCCCTCGGGCCCGACCCGCCAGGAAAGACTG
AGGCCGCGGCCTGCCCCGCCCCGGCTCCCTGCGCCGCGCGCCTCCCGGGACAGAAGATGTG
CTCCAGGGTCCCTCTGCTGCTGCCGCTGCTCCTGCTACTGGCCCTGGGGCCTGGGGTGCAGG
GCTGCCCATCCGGCTGCCAGTGCAGCCAGCCACAGACAGTCTTCTGCACTGCCCGCCAGGGG
ACCACGGTGCCCCGAGACGTGCCACCCGACACGGTGGGGCTGTACGTCTTTGAGAACGGCAT
CACCATGCTCGACGCAGGCAGCTTTGCCGGCCTGCCGGGCCTGCAGTCTCTGGACCTGTAC
AGAACCAGATCGCCAGCCTGCCCAGCGGGGTCTTCCAGCCACTCGCCAACCTCAGCAACCTG
GACCTGACGGCCAACAGGCTGCATGAAATCACCAATGAGACCTTCCGTGGCCTGCGGCGCCT
CGAGCGCCTCTACCTGGGCAAGAACCGCATCCGCCACATCCAGCCTGGTGCCTTCGACACGC
TCGACCGCCTCCTGGAGCTCAAGCTGCAGGACAACGAGCTGCGGGCACTGCCCCGCTGCGC
CTGCCCCGCTGCTGCTGCTGGACCTCAGCCACAACAGCCTCCTGGCCCTGGAGCCCGGCAT
CCTGGACACTGCCAACGTGGAGGCGCTGCGGCTGGCTGGTCTGGGGCTGCAGCAGCTGGACG
AGGGGCTCTTCAGCCGCTTGCGCAACCTCCAGACCTGGATGTGTCCGACAACAGCTGGAG
CGAGTGCCACCTGTGATCCGAGGCCTCCGGGGCCTGACGCGCCTGCGGCTGGCCGGCAACAC
CCGCATTGCCCAGCTGCGGCCCGAGGACCTGGCCGGCCTGGCTGCCCTGCAGGAGCTGGATG
TGAGCAACCTAAGCCTGCAGGCCCTGCTGGCGACCTCTCGGGCCTCTTCCCCCGCCTGCGG
CTGCTGGCAGCTGCCCCGAACCCCTTCAACTGCGTGTGCCCCCTGAGCTGGTTTGGCCCCCTG
GGTGCGGAGAGCCACGTCACTGGCCAGCCCTGAGGAGACGCGCTGCCACTTCCCCCCCA
AGAACGCTGGCCGGCTGCTCCTGGAGCTTGACTACGCCGACTTTGGCTGCCACACCACC
ACCACAGCCACAGTGCCCAACCACGAGGCCCTGGTGGTGCGGGAGCCACAGCCTTGTCTTAG
CTTGGCTCCTACCTGGCTTAGCCCCACAGCGCCGCCACTGAGGCCCCAGCCCCGCTCCA
CTGCCCCACCGACTGTAGGGCCTGTCCCCAGCCCCAGGACTGCCACCGTCCACCTGCCTC
AATGGGGGCACATGCCACCTGGGGACACGGCACCACTGGCGTGCTTGTGCCCCGAAGGCTT
CACGGGCCTGTACTGTGAGAGCCAGATGGGGCAGGGGACACGGCCAGCCCTACACCAGTCA
CGCCGAGGCCACCACGGTCCCTGACCCTGGGCATCGAGCCGTGAGCCCCACCTCCCTGCGC
GTGGGGCTGCAGCGCTACCTCCAGGGGAGCTCCGTGACGCTCAGGAGCCTCCGTCTCACCTA
TCGCAACCTATCGGGCCCTGATAAGCGGCTGGTGACGCTGCGACTGCCTGCCTCGCTCGCTG
AGTACACGGTCACCCAGCTGCGGCCAACGCCACTTACTCCGTCTGTGTATGCCTTTGGGG
CCCCGGGGGTGCCGAGGGCGAGGAGGCTGCGGGGAGGGCCATACACCCCGAGCCGTCCA
CTCCAACCGACGCCCCAGTCACCCAGGCCCGCGAGGGCAACCTGCCGCTCCTCATTGCGCCG
CCCTGGCCGCGGTGCTCCTGGCCGCGCTGGCTGCGGTGGGGGAGCCTACTGTGTGCGGCGG
GGGCGGGCCATGGCAGCAGCGGCTCAGGACAAAGGGCAGGTGGGGCCAGGGGCTGGGCCCT
GGAACCTGGAGGGAGTGAAGGTCCCCTTGGAGCCAGGCCCGAAGGCAACAGAGGGCGGTGGAG
AGGCCCTGCCACGCGGTCTGAGTGTGAGGTGCCACTCATGGGCTTCCAGGGCCTGGCCTC
CAGTCACCCCTCCACGCAAGCCCTACATCTAAGCCAGAGAGAGACAGGGCAGCTGGGGCCG
GGCTCTCAGCCAGTGAGATGGCCAGCCCCCTCCTGCTGCCACACCACGTAAGTTCTCAGTCC
CAACCTCGGGGATGTGTGCAGACAGGGCTGTGTGACCACAGCTGGGCCCTGTTCCCTCTGGA
CCTCGGTCTCCTCATCTGTGAGATGCTGTGGCCCCAGCTGACGAGCCCTAACGTCCCCAGAAC
CGAGTGCCATGAGGACAGTGTCCGCCCTGCCCTCCGCAACGTGCAGTCCCTGGGCACGGCG
GGCCCTGCCATGTGCTGGTAACGCATGCCTGGGTCCCTGCTGGGCTCTCCCACTCCAGGCGGA
CCCTGGGGGCCAGTGAAGGAAGCTCCCGGAAAGAGCAGAGGGAGAGCGGGTAGGCGGCTGTG
TGACTCTAGTCTTGGCCCCAGGAAGCGAAGGAACAAAAGAACTGGAAAGGAAGATGCTTTA
GGAACATGTTTTGCTTTTTTAAATATATATATTTATAAGAGATCCTTTCCCATTTATTCTG
GGAAGATGTTTTCAAACCTCAGAGACAAGGACTTTGGTTTTTGTAAAGACAAACGATGATATG
AAGGCCTTTTGTAAAGAAAAAATAAAGATGAAGTGTGAAA

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FIGURE 32

MCSRVP LLLP LLLLLLALGPGVQGCPSGCQCSQPQT V FCTARQGT TVPRDVPPDTVGLYVFEN
GITMLDAGSFAGLPGLQLLDLSQNQIASLPSGVFQPLANLSNLDLTANRLHEITNETFRGLR
RLERLYLGKNRIRHIQPGAFDTLDRLLELKLQDNELRALPPLRLPRLLLLDLSHNSLLALEP
GILDTANVEALRLAGLG LQQLDEGLFSRLRNLDLDVSDNQLERVPPVIRGLRGLTRLRLAG
NTRIAQLRPEDLAGLAALQELDVS NLSLQALPGDLSGLFPRLRLAAARNPFNCVCPLSWFG
PWVRESHVTIASPEETRCHFPKNAGRLLLELDYADFGCPATTTTATVPTTRPVVREPTALS
SSLAPT WLSPTAPATEAPSPSTAPPTVGPVPQPDCCPSTCLNGGTCHLGTRHHLACLCPE
GFTGLYCESQMGQGTRPSPTPVTPRPRLSLTLGIEPVSPSTSLRVGLQRYLQGS SVQLRSLRL
TYRNLSGPDKRLVTLRLPASLA EYTVTQLRPNATYSVCVMPLGPGRVPEGEEACGEAHTPPA
VHSNHAPVTQAREGNLPLLIAPALAAVLLAALAAVGAAYCVRRGRAMAAAAQDKGQVGPAG
PLELEGVKVPLEPGPKATEGGGEALPSGSECEVPLMGFPGLQSPLHAKPYI

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FIGURE 33

GAATCATCCACGCACCTGCAGCTCTGCTGAGAGAGTGAAGCCGTGGGGGTTTTGAGCTCAT
CTTCATCATTTCATATGAGGAAATAAGTGGTAAAAATCCTTGGAATACAAATGAGACTCAACAG
AAACATTTACATATTTTGTAGTATTGTTATGACAGCAGAGGGTGATGCTCCAGAGCTGCCAG
AAGAAAGGGAACCTGATGACCAACTGCTCCAACATGTCTCTAAGAAAGGTTCCCGCAGACTTG
ACCCAGCCACAACGACACTGGATTTATCCTATAACCTCCTTTTTCAACTCCAGAGTTCAGA
TTTTTATTCTGTCTCCAACTGAGAGTTTTGATTCTATGCCATAACAGAATTCAACAGCTGG
ATCTCAAAACCTTTGAATTCACAAGGAGTTAAGATATTTAGATTTGTCTAATAACAGACTG
AAGAGTGTAACCTGGTATTTACTGGCAGGTCTCAGGTATTTAGATCTTTCTTTAATGACTT
TGACACCATGCTTATCTGTGAGGAAGCTGGCAACATGTACACCTGGAAATCCTAGGTTTGA
GTGGGGCAAAAATACAAAATCAGATTTCCAGAAAATTGCTCATCTGCATCTAAATACTGTC
TTCTTAGGATTGAGAACTCTTCCTCATTATGAAGAAGGTAGCCTGCCCATCTTAAACACAAC
AAAATGACATTTGTTTACCAATGGACACAAATTTCTGGGTTCTTTTGCGTGATGGAATCA
AGACTTCAAAAATATTAGAAATGACAAATATAGATGGCAAAAGCCAATTTGTAAGTTATGAA
ATGCAACGAAATCTTAGTTTAGAAAATGCTAAGACATCGGTTCTATTGCTTAATAAAGTTGA
TTTACTCTGGGACGACCTTTTCTTATCTTACAATTTGTTTGGCATAACATCAGTGGAACT
TTCAGATCCGAAATGTGACTTTTGGTGGTAAGGCTTATCTTGACCACAATTCAATTTGACTAC
TCAAATACTGTAATGAGAACTATAAAATTTGGAGCATGTACATTTAGAGTGTTTTACATTCA
ACAGGATAAAATCTATTTGCTTTTGACCAAAATGGACATAGAAAACCTGACAATATCAAATG
CACAAATGCCACACATGCTTTTCCCGAATTATCTACGAAATTCGAATTTAAATTTTGCC
AATAATATCTTAACAGACGAGTTGTTTAAAAGAACTATCCAACCTGCCTCACTTGAAAATCT
CATTTTGAATGGCAATAAACTGGAGACACTTTCTTAGTAAGTTGCTTTGCTAACAACACAC
CCTTGGAACACTTGGATCTGAGTCAAAATCTATTACAACATAAAAATGATGAAAATTTGCTCA
TGGCCAGAACTGTGGTCAATATGAATCTGTCTACATACAATAAATTGTCTGATTCTGTCTTCAG
GTGCTTGCCCAAAAGTATTCAAATACTTGACCTAAATAATAACCAAAATCCAACTGTACCTA
AAGAGACTATTCTGATGGCCTTACGAGAACTAAATATTGCATTTAATTTCTAACTGAT
CTCCCTGGATGCAGTCATTTAGTAGACTTTAGTTCTGAACATTGAAATGAACTTCATTCT
CAGCCCATCTCTGGATTTGTTTCAGAGCTGCCAGGAAGTTAAACTCTAAATGCGGGAAGAA
ATCCATTCCGGTGTACCTGTGAATTAATAAATTTTCAATTCAGCTTGAAACATATTTCAGAGGT
ATGATGGTTGGATGGTTCAGATTCATACACCTGTGAATACCTTTAAACCTAAGGGGAAGTAG
GTTAAAAGACGTTTCATCTCCACGAATTATCTTGCAACACAGCTCTGTTGATTGTCAACATTG
TGTTATTATGCTAGTTCTGGGGTTGGCTGTGGCCTTCTGCTGTCTCCACTTTGATCTGCCC
TGGTATCTCAGGATGCTAGGTCAATGCACACAAACATGGCACAGGTTAGGAAAACAACCCA
AGAACAACCTCAAGAGAAATGTCCGATTCCACGCATTTATTTTATACAGTGAACATGATTCTC
TGTGGGTGAAGAATGAATTGATCCCCAATCTAGAGAAGGAAGATGGTTCTATCTTGATTGTC
CTTTATGAAAGCTACTTTGACCCTGGCAAAAGCATTAGTGAAAATATTGTAAGCTTCATTGA
GAAAAGCTATAAGTCCATCTTTGTTTTGTCTCCCACTTTGTCCAGAATGAGTGGTGCCATT
ATGAATTTACTTTTGCCCAACCAATCTCTCCATGAAAATTTCTGATCATATAATCTTATC
TTACTGGAAACCCATTCCATTCTATTGCATTCCACCAGGTATCATAAACTGAAAGCTCTCCT
GGAAAAAAGCATACTTGGAAATGGCCCAAGGATAGGCGTAAATGTGGGCTTTTCTGGGCAA
ACCTTCGAGCTGCTATTAATGTTAATGTATTAGCCACCAGAGAAATGTATGAACTGCAGACA
TTCACAGAGTTAAATGAAGAGTCTCGAGGTTCTACAATCTCTCTGATGAGAACAGATTGTCT
ATAAATCCCAAGTCTTTGGGAAGTTGGGGACCACATACACTGTTGGGATGTACATTGATA
CAACCTTTATGATGGCAATTTGACAATATTTATTAATAAATAAATAAATGGTTATTCCCTTCATA
TCAGTTTCTAGAAGGATTTCTAAGAAATGTATCTTATAGAAACACCTTCACAAGTTTATAAGG
GCTTATGGAAGGAGGTGTTTCATCCAGGATTGTTTATAATCATGAAAATGTGGCCAGGTGC
AGTGGCTCACTCTTGTAATCCCAGCACTATGGGAGGCCAAGGTGGGTGACCCACGAGGTCAA
GAGATGGAGACCATCTTGCCCAACATGGTGAAACCTGTCTCTACTAAAAATACAAAAATTA
GCTGGGCGTGATGGTGCACGCCTGTAGTCCCAGCTACTTGGGAGGCTGAGGCAGGAGAATCG
CTTGAACCCGGGAGGTGGCAGTTGCAGTGAGCTGAGATCGAGCCACTGCACTCCAGCCTGGT
GACAGAGCGGAGACTCCATCTCAAAAAAAGAAAAAAGAAAAAATGGAAAAATCC
TCATGGCCACAAAAAAGGTCTAATTCAATAAATTATAGTACATTAAATGTAATATAATTA
CATGCCACTAAAAAAGAAATAAGGTAGCTGTATATTTCTGGTATGGAAAAAATATAATAT
GTTATAAACTATTAGGTTGGTGCAAACTAATTGTGGTTTTTGGCATTGAAATGGCATTGAA
ATAAAGTGTAAAGAAATCTATACCAGATGTAGTAACAGTGGTTTGGGTCTGGGAGGTTGGA
TTACAGGGAGCATTGATTTCTATGTTGTGTAATTTCTATAATGTTTGAATGTTTAGAATGA
ATCTGTATTTCTTTTATAAGTAGAAAAAATAAAGATAGTTTTTACAGCCT

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FIGURE 34

MRLIRNIYIFCSI VMTAEGDAPELPEERELMTNCSNMSLRKVPADLTPATTTLDLSYNLLFQ
LOSSDFHSVSKLRVLILCHNRIQQDLKTFEFNKELRYLDLSNNRLKSVTWYLLAGLRYLDL
SFNDFDTMPICEEAGNMSHLEILGLSGAKIQKSDFQKIAHLHLNTVFLGFRTLPHYEEGSLP
ILNTTKLHIVLPMDTNFWVLLRDGIKTSKILEMTNIDGKSQFVSYEMQRNLSLENAKTSVLL
LNKVDLLWDDLFLILQFVWHTSVEHFQIRNVTFGGKAYLDHNSFDYSNTVMRTIKLEHVHFR
VFYIQQDKIYLLLTCKMDIENLTISNAQMPHMLFPNYPTKFQYLNFANNILTDELFKRTIQLP
HLKTLILNGNKLETLSLVSCFANNTPLEHLDLSONLLQHKNDENCSWPETVVNMNLSYNKLS
DSVFRCLPKSIQILDNNNQIQTPKETIHLMALRELNIAFNFLTDLPGCSHFSRLSVLNIE
MNFILSPSLDFVQSCQEVKTLNAGRNPFRCTCELKNFIQLETYSEVMMVGWSDSYTCEYPLN
LRGTRLKDVHLHELSCNTALLIVTIVVIMLVGLAVAFCCLHFDLPWYLRMLGQCTQTWHRV
RKTTQEQLKRNVRFHAFISYSEHDSLWVKNELIPNLEKEDGSILICLYESYFDPGKSISENI
VSFIEKSYKSIFVLSPNFVQNEWCHYEFYFAHNLFHENS DHIIILILLEPIPFYCIPTRYHK
LKALLEKKAYLEWPKDRRKCGLFWANLRAAINVNVLATREMYELQTFTELNEESRGSTISLM
RTDCL

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FIGURE 35A

GGGGGCTTTCTTGGGCTTGGCTGCTTGGAAACACCTGCCTCCAAGGACCGGCCTCGGAGGGGT
CGCCGGGAAAGGGAGGGAAGAAGGAAGGGCGGGGCCGGCCCCCTGCGCCCCGCCCGCCCT
CTGCGCGCCCCCTGTCCGCCCCGGCCCCAGCCAGCCAGCCCCGCGGGCCGGTCAACACGCGCA
GCCAGCCGGCCGCTCCCGCGCCCCAAGCGCGCCGCTCTGCTGTGCCCTGCGCCCTTGCCCCG
CGCCAGCTTCTGCGCCCCGAGCCCCGCCGGCGCCCCCGGTGACCGTGACCTGCCCTGGGCG
CGGGGCGGAGCAGGCATGTCCCCGCCGGGACCGCTACCCAGCGCTGGCCCTGGTGCTCCT
GGCAGTGACCTGGCCGGGTGCGAGCCAGGGCGCAGCCCTCGAGGACCTGATTATTACG
GGCAGGAGATCTGGAGCCGGGAGCCCTACTACGCGCGCCCGAGCCGAGCTCGAGACCTTC
TCTCCGCCGCTGCTGCGGGGCCGGGGAGGAGTGGGAGCGGCGCCCGAGGAGCCAGGCC
GCCCCAAGAGGGCCACCAAGCCCCAAGAAAGCTCCCCAAGAGGGAGAAGTCGGCTCCGGAGCCGC
CTCCACCAGGTAAACACAGCAACAAAAAAGTTATGAGAACCAAGAGCTCTGAGAAGGCTGCC
AACGATGATCACAGTGTCGTGTGGCCCCGTGAAGATGTGAGAGAGAGTTGCCACCTCTTGG
TCTGGAAACCTTAAAAATCACAGACTTCCAGCTCCATGCCTCCACGGTGAAGCGCTATGGCC
TGGGGGCACATCGAGGGGAGACTCAACATCCAGGCGGGCATTAAATGAAAATGATTTTTATGAC
GGAGCGTGGTGCGCGGGAAGAAATGACCTCCAGCAGTGGATTGAAGTGGATGCTCGGCGCCT
GACCAGATTCACTGGTGTCTCACTCAAGGGAGGAACTCCCTCTGGCTGAGTGACTGGGTGA
CATCCTATAAGGTCATGGTGAGCAATGACAGCCACACGTGGGTCACTGTTAAGAATGGATCT
GGAGACATGATATTTGAGGGAAACAGTGAGAAGGAGATCCCTGTTCTCAATGAGCTACCCGT
CCCCATGGTGGCCCCGTACATCCGCATAAACCCCTCAGTCCTGGTTTTGATAATGGGAGCATCT
GCATGAGAATGGAGATCCTGGGCTGCCACTGCCAGATCCTAATAATTATTATCACCGCCGG
AACGAGATGACCACCACTGATGACCTGGATTTTAAGCACCACAATTATAAGGAAATGCGCCA
GTTGATGAAAGTTGTGAATGAAATGTGTCCCAATATCACCAGAATTTACAACATTGGAAAAA
GCCACCAGGGCCTGAAGCTGTATGCTGTGGAGATCTCAGATCACCCTGGGGAGCATGAAGTC
GGTGAGCCCGAGTTCCACTACATCGCGGGGGCCCCACGGCAATGAGGTGCTGGGCCGGGAGCT
GCTGCTGCTGCTGGTGAGTTTCGTGTGTGAGGAGTACTTGGCCCCGAATGCGCGCATCGTCC
ACCTGGTGGAGGAGACGCGGATTACGTCCTCCCCTCCCTCAACCCCGATGGCTACGAGAAG
GCCTACGAAGGGGGCTCGGAGCTGGGAGGCTGGTCCCTGGGACGCTGGACCCACGATGGAAT
TGACATCAACAACAATTTCTGATTTAAACACGCTGCTCTGGGAGGCAGAGGATCGACAGA
ATGTCCCCAGGAAAGTTCCCAATCACTATATTGCAATCCCTGAGTGGTTTTCTGTGCGAAAT
GCCACGGTGGCTGCCGAGACCAGAGCAGTCATAGCCTGGATGGAAAAAATCCCTTTTGTGCT
GGGCGGCAACCTGCAGGGCGGCGAGCTGGTGGTGGCGTATCCCTACGACCTGGTGCGGTCCC
CCTGGAAGACGCAGGAACACACCCCCACCCCGATGACCACGTGTTCCGCTGGCTGGCCTAC
TCCTATGCCTCCACACACCGCCTCATGACAGACGCCCCGAGGAGGGTGTGCCACACGGAGGA
CTTCCAGAAGGAGGAGGGCACTGTCAATGGGGCCTCCTGGCACACCGTCGCTGGAAGTCTGA
ACGATTTTCAGCTACCTTCATACAACTGCTTCGAACTGTCCATCTACGTGGGCTGTGATAAA
TACCCACATGAGAGCCAGCTGCCCGAGGAGTGGGAGAATAACCGGGAATCTCTGATCGTGTT
CATGGAGCAGGTTTCATCGTGGCATTAAAGGCTTGGTGAGAGATTACATGGAAAAGGAATCC
CAAACGCCATTATCTCCGTAGAAGGCATTAACCATGACATCCGAACAGCCAACGATGGGGAT
TACTGGCGCCTCCTGAACCTGGAGAGTATGTGGTCACAGCAAAGGCCGAAGGTTTCACTGC
ATCCACCAAGAACTGTATGGTTGGCTATGACATGGGGGCCACAAGGTGTGACTTCACACTTA
GCAAAACCAACATGGCCAGGATCCGAGAGATCATGGAGAAGTTTGGGAAGCAGCCCCGTCAGC
CTGCCAGCCAGGCGCTGAAGCTGCGGGGGCGGAAGAGACGACAGCGTGGGTGAACCTCCTG
GGCCCTTGAGACTCGTCTGGACCCATGCAATTAACCAACCTGGTAGTAGCTCCATAGTG
GACTCACTCACTGTTGTTTCTCTGTAATTCAAGAAGTGCCTGGAAGAGAGGGTGCATTGTG
AGGCAGGTCCCAAAGGGAAGGCTGGAGGCTGAGGCTGTTTTCTTTCTTTGTTCCATTTA
TCCAAATAACTTGACAGAGCAGCAGAGAAAAGCTGATGGGAGTGAGAGAACTCAGCAAGCC
AACCTGGGAATCAGAGAGAGAAGGAGAAGGAGGGGAGCCTGTCCGTTACAGACCTCTGGCTGC

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FIGURE 35B

ATAGAAAAGGATTCTGGTGCTTCCCCTGTTTGCCTGGCAGCAAGGGTTCCACGTGCATTTGC
AATTTGCACAGCTAAAATTGCAGCATTTCCCCAGCTGGGCTGTCCCAAATGTTACCATTTGA
GATGCTCCCAGGCGTCCTAAGAGAATCCACCCTCTCTGGCCCTGGGACATTGCAAGCTGCTA
CAAATAAATTCTGTGTTCTTTTGACAATAGCGTCATTGCCAAGTGCACATCAGTGAGCCTCT
TGAATCTGTTTAGTCTCCTTTTTCAACAAAGGAGTGTTGTTTGCAGAAAAGGAGAGAGAGGCTGA
GATCATTCAGGAGTTTGTGTTGGGAGCAAGCATGGAGCTTCTTGACAAAATTCTGGGTCCATA
AACAAACCCCAAGTCCCTGCTGATCCAGTAGCCCTGGAGGTTCCCCAGGTAGGGAGAGCCA
GAGGTGCCAGCCTTCTGAAGGGCCAGAAAATTTAGCCTGGATCTCCTCTTTTACCTGCTAG
GACTGGAAGAGCCAGAAGTGGGGTGGCCTGAAGCCCTCTCTCTGCTTGAGGTATTGCCCCCT
GTGTGGAATTGAGTGCTCATGGGTGGCCTCATATCAGCCTGGGAGTTATTTTTGATATGTA
GAATGCCAGATCTTCCAGATTAGGCTAAATGTAATGAAAACCTCTTAGGATTATCTGTGGAG
CATCAGTTTGGGAAGAATTATTGAATTATCTTGCAAGAAAAAAGTATGTCTCACTTTTTTGT
AATGTTGCTGCCTCATTGACCTGGGAAAAATGAAAAAAAAAATAAGCAAATGGTAAGACC
CTTAAA

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FIGURE 36

MSRPGTATPALALVLLAVTLAGVGAQGALEDPDYYGQEIWSREPYARPEPELETFSPPLP
AGPGEEWERRPQEPRPPKRATKPKKAPKREKSAPEPPPPGKHSNKKVMRTKSSEKAANDDHS
VRVAREDVRESCPPLGLETLKITDFQLHASTVKRYGLGAHRGRLNIQAGINENDFYDGAWCA
GRNDLQQWIEVDARRLTRFTGVITQGRNSLWLSDWVTSYKVMVSNDSTWVTVKNGSGDMIF
EGNSEKEIPVLNELPVPMPVARYIRINPQSWFDNGSICMRMEILGCPLPDPNNYYHRRNEMTT
TDDLDFKHHNYKEMRQLMKVVNEMCPNITRIYNIGKSHQGLKLYAVEISDHPGEHEVGEPEF
HYIAGAHGNEVLGRELLLLLVQFVCQEYLARNARIVHLVEETRIHVLPSLNPDGYEKAYEGG
SELGGWSLGRWTHDGIDINNNFPDLNTLLWEAEDRQNVPRKVPNHYIAIPEWFLSENATVAA
ETRAVIAWMEKIPFVLGGNLQGGELVVAYPYDLVRSPWKTQEHTPTPDDHVFRWLAYSAST
HRLMTDARRRVCHTEDFQKEEGTVNGASWHTVAGSLNDFSYLHTNCFELSIIYVGCDKYPHES
QLPEEWENNRESLIVFMEQVHRGIKGLVRDSHGKGI PNAIISVEGINHDIRTANDGDYWRLL
NPGEYVVTAKAEGFTASTKNCMVG YDMGATRCDFTL SKTNMARI REIMEKFGKQPVSLPARR
LKLGRKRQRG

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FIGURE 37

CTAAGAGGACAAGATGAGGCCCGGCTCTCATTCTCTCTAGCCCTTCTGTTCTTCTCTTGCC
AAGCTGCAGGGGATTTGGGGGATGTGGGACCTCCAATTCCCAGCCCCGGCTTCAGCTCTTTC
CCAGGTGTTGACTCCAGCTCCAGCTTCAGCTCCAGCTCCAGGTGCGGCTCCAGCTCCAGCCG
CAGCTTAGGCAGCGGAGGTTCTGTGTCCAGTTGTTTTCCAATTTACCGGCTCCGTGGATG
ACCGTGGGACCTGCCAGTGCTCTGTTTCCCTGCCAGACACCACCTTTCCCGTGGACAGAGTG
GAACGCTTGGAATTCACAGCTCATGTTCTTTCTCAGAAGTTTGAGAAAGAACTTTCTAAAGT
GAGGGAATATGTCCAATTAATTAGTGTGTATGAAAAGAACTGTTAAACCTAACTGTCCGAA
TTGACATCATGGAGAAGGATACCATTTCTTACACTGAACTGGACTTCGAGCTGATCAAGGTA
GAAGTGAAGGAGATGGAAAACTGGTCATACAGCTGAAGGAGAGTTTTGGTGGAAGCTCAGA
AATTGTTGACCAGCTGGAGGTGGAGATAAGAAATATGACTCTCTGGTAGAGAAGCTTGAGA
CACTAGACAAAAACAATGTCCTTGCCATTGCGCGAGAAATCGTGGCTCTGAAGACCAAGCTG
AAAGATGTTGAGGCCTCTAAAGATCAAAACACCCCTGTCTGCCACCTCCTCCACTCCAGG
GAGCTGTGGTCATGGTGGTGGTGAACATCAGCAAACCGTCTGTGGTTCACTCAACTGGA
GAGGTTTTCTTATCTATATGGTGCTTGGGGTAGGGATTACTCTCCCAGCATCCAAACAAA
GGACTGTATTGGGTGGCGCCATTGAATACAGATGGGAGACTGTTGGAGTATTATAGACTGTA
CAACACACTGGATGATTTGCTATTGTATATAAATGCTCGAGAGTTGCGGATCACCTATGGCC
AAGGTAGTGGTACAGCAGTTTACAACAACAACATGTACGTCAACATGTACAACACCGGGAAT
ATTGCCAGAGTTAACTGACCACCAACACGATTGCTGTGACTCAAACCTCTCCCTAATGCTGC
CTATAATAACCGCTTTTCATATGCTAATGTTGCTTGGCAAGATATTGACTTTGCTGTGGATG
AGAATGGATTGTGGGTTATTTATTCAACTGAAGCCAGCACTGGTAACATGGTGATTAGTAAA
CTCAATGACACCACACTTCAGGTGCTAAACACTTGGTATACCAAGCAGTATAAACCATCTGC
TTCTAACGCCTTCATGGTATGTGGGTTCTGTATGCCACCCGTAATGAACACCAGAACAG
AAGAGATTTTTTACTATTATGACACAAACACAGGGAAAGAGGGCAAACCTAGACATTGTAATG
CATAAGATGCAGGAAAAAGTGCAGAGCATTAACTATAACCCTTTTGACCAGAACTTTATGT
CTATAACGATGGTTACCTTCTGAATTATGATCTTTCTGTCTTGCAAGCCCCAGTAAAGCTG
TTTAGGAGTTAGGGTGAAAGAGAAAAATGTTTGTGAAAAAATAGTCTTCTCCACTTACTTAG
ATATCTGCAGGGGTGTCTAAAAGTGTGTTTCAATTTTGAGCAATGTTTAGGTGCATAGTTCTA
CCACACTAGAGATCTAGGACATTTGTCTTGATTTGGTGAGTTCTCTGGGAATCATCTGCCT
CTTCAGGCGCATTTTGCAATAAAGTCTGTCTAGGGTGGGATTGTGAGAGTCTAGGGGCACT
GTGGGCCTAGTGAAGCCTACTGTGAGGAGGCTTCACTAGAAGCCTTAAATTAGGAATTAAGG
AACTTAAAACTCAGTATGGCGTCTAGGGATTCTTTGTACAGGAAATATTGCCCAATGACTAG
TCCTCATCCATGTAGCACCCTAATTCTTCCATGCCTGGAAGAAACCTGGGGACTTAGTTAG
GTAGATTAATATCTGGAGCTCCTCGAGGGACCAAATCTCCAACCTTTTTTTTCCCCTCACTAG
CACCTGGAATGATGCTTTGTATGTGGCAGATAAGTAAATTTGGCATGCTTATATATTCTACA
TCTGTAAAGTGTGAGTTTATGGAGAGAGGCCTTTTTATGCATTAAATTGTACATGGCAAA
TAAATCCCAGAAGGATCTGTAGATGAGGCACCTGCTTTTTCTTTCTCTCATTGTCCACCTT
ACTAAAAGTCAGTAGAATCTTCTACCTCATAACTTCCTTCCAAAGGCAGCTCAGAAGATTAG
AACCAGACTTACTAACCAATCCACCCCCCACCACCCCTTCTACTGCCTACTTTAAAAAA
ATTAATAGTTTTCTATGGAAGTATCTAAGATTAGAAAAATTAATTTTCTTTAATTTCTTA
TGGACTTTTATTTACATGACTCTAAGACTATAAGAAAACTGTATGGCAGTGACAAAGTGCTA
GCATTTATTGTTATCTAATAAGACCTTGGAGCATATGTGCAACTTATGAGTGTATCAGTTG
TTGCATGTAATTTTTGCCTTTGTTTAAAGCCTGGAACCTGTAAGAAAAATGAAAATTTAATTTT
TTTTTCTAGGACGAGCTATAGAAAAGCTATTGAGAGTATCTAGTTAATCAGTGCAGTAGTTG
GAAACCTTGCTGGTGTATGTGATGTGCTTCTGTGCTTTTGAATGACTTTATCATCTAGTCTT
TGTCTATTTTTCTTTGATGTTCAAGTCCTAGTCTATAGGATTGGCAGTTTAAATGCTTTAC
TCCCCCTTTTAAATAAATGATTAAATGTGCTTTGAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 38

MRPGLSFLLALLFFLGQAAGDLGDVGPPIPSPGFSSFPGVDSFFFSSSSSRSGSSSSRSLGS
GGSVSQLF SNFTGSVDDRGTCCQCSVSLPDTTFPVDRVERLEFTAHVLSQKFEKELSKVREYV
QLISVYEKKLLNLTVRIDIMEKDTISYTELDFELIKVEVKEMEKLVIQLKESFGGSSEIVDQ
LEVEIRNM TLLVEKLETLDKNNVLAIRREIVALKTKLKECEASKDQNTPVVHPPPTPGSCGH
GGVWNISKPSVVQLNWRGFSYLYGAWGRDYSPQHHPNKGLYWVAPLNTDGRLLLEYRLYNTLD
DLLLLYINARELRITYGQSGTAVYNNNMYVNMVNTGNIARVNLTNTIAVTQTLPNAAAYNNR
FSYANVAWQDIDFAVDENGLWVIYSTEASTGNMVISKLNDTTLQVLNTWYTKQYKPSASNAF
MVCGLVYATRMTMNRTEEIFYYYDTNTGKEGKLDIVMHKMQEKVQSINYNPFDQKLYVYNDG
YLLNYDLSVLQKPQ

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FIGURE 39

GCTCTGAAGACCAAGCTGAAAGAGTGTGAGGCCTCTAAAGATCAAACACCCCTGTGCTCCAC
CCTCCTCCCACTCCAGGGAGCTGTGGTCATGGTGGTGTGGTGAACATCAGCAAACCGTCTGT
GGTTCAGCTCAACTGGAGAGGGTTTTCTTATCTATATGGTGCTTGGGGTAGGGATTACTCTC
CCCAGCATCCAAACAAAGGNATGTATTGGGNGGCGCCATTGAATACAGATGGGAGACTGTTG
GAGTATTATAGACTGTACAACCCACTGGATGATTTGCTATTGTATATAAATGCTCGAGAGTT
GCGGATCACCTATGGCCAAGGTAGTGGTACAGCAGTTTACAACAACAACATGTACGTCAACA
TGTACAACACCGGNATATTGCCAGAGTTAACCTGACC

FIGURE 40

TCTCGCAGATAGTAAATAATCTCGGAAAGGCGAGAAAGAAGCTGTCTCCATCTTGTCTGTAT
CCGCTGCTCTTGTGACGTTGTGGAGATGGGGAGCGTCCTGGGGCTGTGCTCCATGGCGAGCT
GGATACCATGTTTGTGTGGAAGTGCCCGTGTTTGTCTATGCCGATGCTGTCCTAGTGGAAC
AACTCCACTGTAACTAGATTGATCTATGCACTTTTCTTGCTTGTGGAGTATGTGTAGCTTG
TGTAATGTTGATACCAGGAATGGAAGAACAACCTGAATAAGATTCTGGATTTTGTGAGAATG
AGAAAGGTGTTGTCCCTTGTAACTTTTGGTTGGCTATAAAGCTGTATATCGTTTGTGCTTT
GGTTTGGCTATGTTCTATCTTCTTCTCTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGA
TCCTAGAGCTGCAGTGCACAATGGATTTTGGTTCTTTAAATTTGCTGCAGCAATTGCAATTA
TTATTGGGGCATTCTTCATTCCAGAAGGAACCTTTACAACCTGTGTGGTTTTATGTAGGCATG
GCAGGTGCCTTTTGTTCATCCTCATACAACCTAGTCTTACTTATTGATTTTGCACATTCATG
GAATGAATCGTGGGTTGAAAAAATGGAAGAAGGGAACCTCGAGATGTTGGTATGCAGCCTTGT
TATCAGCTACAGCTCTGAATTATCTGCTGTCTTTAGTTGCTATCGTCTGTCTTTTGTCTAC
TACACTCATCCAGCCAGTTGTTTCAAGAAACAAGGCGTTTCATCAGTGTCAACATGCTCCTCTG
CGTTGGTGCTTCTGTAATGTCTATACTGCCAAAAATCCAAGAATCACAACCAAGATCTGGTT
TGTTACAGTCTTTCAGTAATTACAGTCTACACAATGTATTTGACATGGTCAGCTATGACCAAT
GAACCAGAAACAATTTGCAACCCCAAGTCTACTAAGCATAATTGGCTACAATACAACAAGCAC
TGTCCCAAAGGAAGGGCAGTCAGTCCAGTGGTGGCATGCTCAAGGAATTATAGGACTAATTC
TCTTTTTGTTGTGTGTATTTTATTCCAGCATCCGTACTTCAAACAATAGTCAGGTTAATAAA
CTGACTCTAACAAGTGATGAATCTACATTAATAGAAGATGGTGGAGCTAGAAGTGATGGATC
ACTGGAGGATGGGGACGATGTTTCAACGAGCTGTAGATAATGAAAGGGATGGTGTCACTTACA
GTTATTCTTCTTTCACTTCATGCTTTTCTGGCTTCACTTTATATCATGATGACCTTTACC
AACTGGTCCAGGTATGAACCTCTCGTGAGATGAAAAGTCAGTGGACAGCTGTCTGGGTGAA
AATCTCTTCCAGTTGGATTGGCATCGTGTGTATGTTTGGACACTCGTGGCACCCTTGTTC
TTACAAATCGTGATTTTGAAGTGAAGTACTTCTAGCATGAAAGTCCCCTTTGATTATTGC
TTATTTGAAAACAGTATTTCCCACTTTTGTAAAGTTGTGTATGTTTTTGGCTTCCCATGTAAC
TTCTCCAGTGTTCTGGCATGAATTAGATTTTACTGCTTGTCAATTTTGTATTTTCTTACCAA
GTGCATTGATATGTGAAGTAGAATGAATTGCAGAGGAAAGTTTTATGAATATGGTGATGAGT
TAGTAAAGTGGCCATTATTGGGCTTATTCTCTGCTCTATAGTTGTGAAATGAAGAGTAAAA
ACAAATTTGTTTGAATTTTAAAATTATATTAGACCTTAAGCTGTTTTAGCAAGCATTAAA
GCAAATGTATGGCTGCCTTTTGAATATTTGATGTGTTGCCTGGCAGGATACTGCAAGAAC
ATGGTTTATTTTAAAATTTATAACAAGTCACTTAAATGCCAGTTGTCTGAAAAATCTTATA
AGGTTTTACCCTTGATACGGAATTTACACAGGTAGGGAGTGTAGTGGACAATAGTGTAGGTTA
TGGATGGAGGTGTCGGTACTAAATGAATAACGAGTAAATAATCTTACTTGGGTAGAGATGG
CCTTTGCCAACAAAGTGAAGTGTGTTTGGTTGTTTTAACTCATGAAGTATGGGTTTCACTGGA
AATGTTTTGGAAGTCTGAAGGATTTAGACAAGGTTTTGAAAAGGATAATCATGGGTTAGAAGG
AAGTGTGTTTGAAGTCACTTTGAAAGTTAGTTTTGGGCCAGCACGGTAGCTCACCTTGGT
AATCCCAGCACTTTGGGAGCTTAAGTGGGTAGATTACTTGAGCCAGGAATTCAGACCAGCT
TGGCACATGGTGAACCTGTTCTATAAAAAATAATCTGGCTTTGAGCATATGCCTGTGGTCCAG
CACTGAGAGGCTAGTGAAGATTGCTGAGCCCAGAGCCAAAGGTTGCAGTGAGCAAGTCACGT
CACTGCACTCTAGCTGGCACAGAGTAAGCCAAAAAATATATATATATTGAAATCAAGGAGG
CAAAATTTTGAAGGGAAGGAAGTAAGTCAAAACCACTAGGCTTTAGTAGGTACTTATATA
AAATCTAGTCCAGTTCTCTCATTTAAAAAATGAAGCACTGAAATACAGACTTAAATAGCT
CAGATAGCTAATTAGGAAATTTCAAGTTGGCCAATAATAGCATTCTCTGACATTTAAAAA
TAATTTCTATTCAAATAACATGCATATTGATTTACACCTCATACTGTGATAATTAATGTGAT
GTGGATTGCTGGTGTCCAGCATGACCCATAAACAGGTGAGAAGAATGATGGAATGTTTTAGA
ATAAACTCCTGCTTATAGTATACTACACAGTTCAAAGATGTTTAAATGCTTTTGTATTTA
CTGCCATGTAATTGAAATATATAGATTATTGTAACCTTTCAACCTGAAAATCAAGCAGTATG
AGAGTTTAGTTATTGTATGTGTCACTAGTGTCTAATGAAGCTTTTAAATCTACAATTTCT
TCTTTAAAAATATTTATTAATGTGAATGGAATATAACAATTCAGCTTAATCCCCAACCTTA
TTCTGTGTGTAGACATTGTATTCCACAATTTTGAATGGCTGTGTTTTACCTCTAAATAAATG
AATTCAGAGAAAAA

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FIGURE 41

MGSVLGLCSMASWIPCLCGSAPCLLCRCCPSGNNSTVTRLIYALFLLVGVCVACVMLIPGME
EQLNKIPGFCENEKGVVPCNILVGKYKAVYRLCFGLAMFYLLLSLLMIKVKSSSDPRAAVHNG
FWFFKFAAAIAIIIGAFFIPEGTFTTVWFYVGMAGAFCFILIQVLVLLIDFAHSWNESWVEKM
EEGNSRCWYAALLSATALNYLLSLVAIVLFFVYYTHPASCSENKAFISVNMLLCVGASVMSI
LPKIQESQPRSGLLQSSVITVYTMYLTSAMTNEPETNCNPSLLSIIGYNTTSTVPKEGQSV
QWWHAQGIIGLILFLLCVFYSSIRTSNNSQVNKLTLTSDESTLIEDGGARSDGSLEDGDDVH
RAVDNERDGVITYSYSFFHFMLFLASLYIMMTLTNWSRYEPSREMKSQWTAVVWKISSSWIGI
VLYVWTLVAPLVLTNRDFD

FIGURE 42

GCGAGAAAGAAGCTGTCTCCATCTTGTCTGTATCCCGCTGCTTCTTGNGACGTTGTGGAGAT
GGGGAGCGTCCCTGGGGCTGTGCTCCATGGCGAGCTGGATAACCATGTTTGTGTGGAAGTGCC
CCGTGTTTGCTATGCCGATGCTGTCCTAGTGGAACAANTCCACTGTAACTAGATTGATCTA
TGCACTTTTCTTGCTTGTGAGTATGTGTAGCTTGTGTAATGTTGATACCAGGAATGGAAG
AACAACTGAATAAGATTCCTGGATTTTGTGAGAATGAGAAAGGTGTTGTCCCTTGTAACATT
TTGGTTGGCTATAAAGCTGTATATCGTTTGTGCTTTGGTTTGGCTATGTTCTATCTTCTTCT
CTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCAGTGCACAATGGAT
TTTGGTTCTTTAAATTTGCTGCAGCAATTGCAATTATTATTGGGGC

FIGURE 43

GTTATTGTGAACTTTGTGGAGATGGGAGGTCNTGGGGCTGTGTTCCATGGCGAGCTGGATAC
CANGTTTGTGTGGAAGTGCCCCGTGTTTGNATATGCCGATGCTGTCCTAGTGGAAACAANTCC
ACTGTAATTAGATTGATNTATGCACTTTTNTTGCTTGTTGGAGTANGTGTAGCTTGTGTAAT
GTTGATACCAGGAATGGAAGAACAACCTGAATAAGATTCCTGGATTTTGTGAGAATGAGAAAG
GTGTTGTCCCTTGTAACATTTTGGTTGGCTATAAAGCTGTATATNGTTTGTGCTTTGGTTTG
GCTANGTTCTATNTTCTTCTCTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAG
AGCTGCAGTGCAATGGATTTTGGTTTTTTAAATTTGCTGCAGCAATTGCAATTATTATTG
GGGC

FIGURE 44

AAGAAGCTGTCTCCATCTTGTCTGTATCCGCTGCTCTTGTGAACGTTNTGGAGATGGGGAGC
GTCCTTGGGGTTG-TGCTCCATGGCGAGCTGGATAACCATGTTTGTGTGGAAAGTGCCCCGTGTT
TGCTATGCCGATGCTGTCCCTAGTGGAACAACCTCCACTGTAACTAGATTGATCTATGCACTT
TTCTTGCTTGTGAGTATGTGTAGCTTGTGTAATGTTGATACCAGGAATGGAAGAACAACCT
GAATAAGATTCCCTGGATTTTGTGAGAATGAGAAAGGTGTTGTCCCTTGTAACATTTTGTTG
GCTATAAAGCTGTATATCGTTTGTGCTTTGGTTTGGCTATGTTCTATCTTCTCTCTTTA
CTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCAGTGCACAATGGATTTTGTT
CTTTAAATTTGCTGCAGCAATTGCAATTATTATTGGGGC

FIGURE 45

GCTGTCCTTAGTGGAACAANTCCAACCTTGTAACCTGGATTGATCTATGCACTTTTTTCCTTG
CTTGTTGGAGTATGTGTAGCTTTGTGTAATGTTGTTCCCAGGATTGGANGAACAACTGAATA
AGATTCCCTGGATTTTTGTGAGAATGAGAAAGGTGTTGTCCCCTTGTAACATTTTTGGTTGGC
TATAAAGCTGTATATCGTTTGTGCTTTGGTTTGGCTATGTTCTATCTTCTTCTCTTTACT
AATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCAGTGCACAATGGATTTTTGGTTCT
TTAAATTTGCTGCAGCAATTGCAATTATTATTGGGGCATTCTTCATTCCAGAAGGAACTTTT
ACAACTGTGTGGTTTTATGTAGGCATGGCAGGTGCCTTTTGTTCATCCTCATACAACTAGT
CTTACTTATTGATTTTGCACATTCATGGAATGAATCGTGGGTGAAAAAATGGAAGAAGGGA
ACTCGAGATGTTGGTATGCAGCCTTGTTATCAGCTACAGCTCTGAATTATCTGCTGTCTTTA
GTTGCTATCGTCCTGTTCTTTGTCTACTACACTCATCCAGCCAGTTGTTTCAGAAAACAAGGC
GTTTCATCAGTGTCAACATGCTCCTCTGCGTTGGTGCTTCTGTAATG

FIGURE 46A

CTCGGGCGCGCACAGGCAGCTCGGTTTGCCCTGCGATTGAGCTGCGGGTCGCGGCCGGCGCC
 GGCTCTCCAATGGCAAATGTGTGTGGCTGGACGCGAGCGCGAGGCTTTCGGCAAAGGCAGT
 CGAGTGTTCAGACCGGGGCGAGTCCTGTGAAAGCAGATAAAAGAAAACATTTATTAACGT
 GTCATTACGAGGGGAGCGCCCGGGCGGGGCTGTGCGACTCCCCGCGGAACATTTGGCTCCCT
 CCAGCTCCGAGAGAGGAGAAGAAGAAAGCGGAAAAGAGGCAGATTCACGTGTTTTCCAGCCA
 AGTGGACCTGATCGATGGCCCTCCTGAATTTATCAGATATTTGATTATTAGCGATGCCCC
 CTGGTTTGTGTGTTACGCACACACAGTGCACACAAGGCTCTGGCTCGCTTCCCTCCCTCGT
 TTCCAGCTCCTGGGCGAATCCACATCTGTTTCAACTCTCCGCCGAGGGCGAGCAGGAGCGA
 GAGTGTGTGGAATCTGCGAGTGAAGAGGGACGAGGGAAAAGAAAACAAAGCCACAGACGCAAC
 TTGAGACTCCCGCATCCCAAAAGAAAGCACCAGATCAGCAAAAAAGAAAGATGGGCCCCCGA
 GCCTCGTGCTGTGCTTGCTGTCCGCAACTGTGTTCTCCCTGCTGGGTGGAAGCTCGGCCTTC
 CTGTGCGACCACCGCCTGAAAGGCAGGTTTCAGAGGGACCGCAGGAACATCCGCCCAACAT
 CATCCTGGTGCTGACGAGCAGACAGGATGTGGAGCTGGGTTCATGCAGGTGATGAACAAGA
 CCCGGCGCATCATGGAGCAGGGCGGGCGCACTTCATCAACGCCTTCGTGACCACACCCATG
 TGCTGCCCTCACGCTCCTCCATCCTCACTGGCAAGTACGTCCACAACCACAACACCTACAC
 CAACAATGAGAACTGCTCCTCGCCCTCCTGGCAGGCACAGCAGAGAGCCGCACCTTTGCCG
 TGTACCTCAATAGCACTGGCTACCGACAGCTTTCTTCGGGAAGTATCTTAATGAATACAAC
 GGCTCCTACGTGCCACCCGGCTGGAAGGAGTGGGTCCGACTCCTTAAAAACTCCCGCTTTTA
 TAACTACACGCTGTGTGGAACGGGGTGAAAGAGAAGCACGGCTCCGACTACTCCAAGGATT
 ACCTCACAGACCTCATACCAATGACAGCGTGAGCTTCTTCCGCACGTCCAAGAAGATGTAC
 CCGCACAGGCCAGTCTCATGGTCATCAGCCATGCAGCCCCCACGGCCCTGAGGATTACG
 CCCACAATATTACGCCTCTTCCCAAACGCATCTCAGCACATCAGCCGAGCTACAACCTACG
 CGCCCAACCCGGACAAACACTGGATCATGCGCTACACGGGGCCCATGAAGCCCCATCCACATG
 GAATTCACCAACATGCTCCAGCGGAAGCGCTTGACAGCCCTCATGTGCGTGGACGACTCCAT
 GGAGACGATTTACAACATGCTGGTTGAGACGGGCGAGCTGGACAACACGTACATCGTATACA
 CCGCCGACCACGGTTACCACATCGGCCAGTTTGGCCCTGGTGAAAGGGAAATCCATGCCATAT
 GAGTTTGACATCAGGGTCCCGTTCTACGTGAGGGGCCCAACGTGGAAGCCGGCTGTCTGAA
 TCCCCACATCGTCTCAACATTGACCTGGCCCCCACCATCCTGGACATTGCAGGCCTGGACA
 TACCTGCGGATATGGACGGGAAATCCATCCTCAAGCTGCTGGACACGGAGCGGCCGTGAAT
 CGGTTTTCACTTGAAAAGAAGATGAGGGTCTGGCGGGACTCCTTCTTGTTGGAGAGAGGCAA
 GCTGCTACACAAGAGAGACAATGACAAGGTGGACGCCAGGAGGAGAACTTTCTGCCCAAGT
 ACCAGCGTGTGAAGGACCTGTGTGAGCGTGTGAGTACCAGACGGCGTGTGAGCAGCTGGGA
 CAGAAGTGGCAGTGTGTGGAGGACGCCACGGGGAAGCTGAAGCTGCATAAGTGCAAGGGCCC
 CATGCGGCTGGGCGGCAGCAGAGCCCTCTCCAACCTCGTGCCCAAGTACTACGGGCAGGGCA
 GCGAGGCCTGCACCTGTGACAGCGGGGACTACAAGCTCAGCCTGGCCGACGCGGGAACAAA
 CTCTTCAAGAAGAAGTACAAGGCCAGCTATGTCCGCAGTCGCTCCATCCGCTCAGTGGCCAT
 CGAGGTGGACGGCAGGGTGTACCACGTAGGCCTGGGTGATGCCGCCAGCCCCGAAACCTCA
 CCAAGCGGCACTGGCCAGGGGCCCTGAGGACCAAGATGACAAGGATGGTGGGGACTTCAGT
 GGCCTGGAGGCCTTCCCGACTACTCAGCCGCCAACCCATTAAAGTGACACATCGGTGCTA
 CATCCTAGAGAACGACACAGTCCAGTGTGACCTGGACCTGTACAAGTCCCTGCAGGCCTGGA
 AAGACCACAAGCTGCACATCGACCACGAGATTGAAACCCTGCAGAACAAAATTAAGAACCTG
 AGGGAAGTCCGAGGTACCTGAAGAAAAGCGGCCAGAAGAATGTGACTGTACAAAATCAG
 CTACCACACCCAGCACAAAGGCCGCTCAAGCACAGAGGCTCCAGTCTGCATCCTTTTCAGGA
 AGGGCCTGCAAGAGAAGGACAAGGTGTGGCTGTTGCGGGAGCAGAAGCGCAAGAAGAACTC
 CGCAAGCTGCTCAAGCGCCTGCAGAACAACGACAGTGCAGCATGCCAGGCCTCACGTGCTT
 CACCCACGACAACAGCACTGGCAGACGGCGCCTTTCTGGACACTGGGGCCTTTCTGTGCCT
 GCACCAGCGCCAACAATAACACGTACTGGTGCATGAGGACCATCAATGAGACTCACAATTC

FIGURE 46B

CTCTTCTGTGAATTTGCAACTGGCTTCCTAGAGTACTTTGATCTCAACACAGACCCCTACCA
GCTGATGAATGCAGTGAACACACTGGACAGGGATGTCCTCAACCAGCTACACGTACAGCTCA
TGGAGCTGAGGAGCTGCAAGGGTTACAAGCAGTGTAACCCCGGACTCGAAACATGGACCTG
GATGGAGGAAGCTATGAGCAATACAGGCAGTTTCAGCGTCGAAAGTGGCCAGAAATGAAGAG
ACCTTCTTCCAAATCACTGGGACAACTGTGGGAAGGCTGGGAAGGTTAAAGAAACAACAGAGG
TGGACCTCCAAAAACATAGAGGCATCACCTGACTGCACAGGCAATGAAAAACCATGTGGGTG
ATTTCCAGCAGACCTGTGCTATTGGCCAGGAGGCCTGAGAAAGCAAGCACGCACTCTCAGTC
AACATGACAGATTCTGGAGGATAACCAGCAGGAGCAGAGATAACTTCAGGAAGTCCATTTTT
GCCCCTGCTTTTGCTTTGGATTATACCTCACCAGCTGCACAAAATGCATTTTTTCGTATCAA
AAAGTCACCACTAACCCCTCCCCCAGAAGCTCACAAAGGAAAAACGGAGAGAGCGAGCGAGAGA
GATTTCTTGGAATTTCTCCCAAGGGCGAAAGTCATTGGAATTTTAAATCATAGGGGAAA
AGCAGTCCTGTTCTAAATCCTCTTATTCTTTTGGTTTGTACAAAGAAGGAACTAAGAAGCA
GGACAGAGGCAACGTGGAGAGGCTGAAAACAGTGCAGAGACGTTTGACAATGAGTCAGTAGC
ACAAAAGAGATGACATTTACCTAGCACTATAAACCCCTGGTTGCCTCTGAAGAAACTGCCTTC
ATTGTATATATGTGACTATTTACATGTAATCAACATGGGAACTTTTAGGGGAACCTAATAAG
AAATCCCAATTTTCAGGAGTGGTGGTGTCAATAAACGCTCTGTGGCCAGTGTAAGAAAAA

FIGURE 47

MGPPSLVLCLLSATVFSLLGGSSAFLSHRLKGRFQRDRRNIRPNI ILVLTDDQDVELGSMQ
VMNKTRRIMEQGGAHFINAFVTTMCCPSRSSILTGKYVHNHNTYTNNECSPSWQAQHE
RTFAVYLNSTGYRTAFFGKYLNEYNGSYVPPGWKEWVGLLKNSRFYNYTLCRNGVKEKHGSD
YSKDYLTDLITNDSVSFFRTSKKMYPHRPVLMVISHAAPHGPEDSAPQYSRLFPNASQHITP
SYNYAPNPDKHWIMRYTGPMKPIHMEFTNMLQRKRLQTLMSVDDSMETIYNMLVETGELDNT
YIVYTADHGYHIGQFGLVKGKSMPYEFDIRVPFYVRGPNVEAGCLNPHIVLNIDLAPTILDI
AGLDIPADM DGKSILKLLDTERPVNRFHLKKKMRVWRDSFLVERGKLLHKRDNDKVDAQEEN
FLPKYQRVKDL CQRAEYQTACEQLGQKWQCVEDATGKLK LHKCKGPMRLGGSRALSNLVPKY
YGQGSEACTCDSGDYKLSLAGRRKKLFKKKYKASYVRSRSIRSV AIEVDGRVYHVGLGDAAQ
PRNLTKRHWPGAPEDQDDKDGGDFSGTGGLPDYSAANPIKVTHRCYILENDTVQCDLDLYKS
LQAWKDHKLHIDHEIETLQNKIKNLREVRGHLKKKRPEECDCHKISYHTQHKGR LKHGSSSL
HPFRKGLQEKDKVWLLREQKRKKLRKLLKRLQNNDTCSMPGLTCFTHDNQHWQTAPFWTLG
PFCACTSANNNTYWCMRTINETHNFLFCFATGFLEYFDLNTDPYQLMNAVNTLDRDVLNQL
HVQLMELRSCKGYKQCNPRTRNMDLDGGSYEQYRQFQRRKWPEMKRPSSKSLGQLWEGWEG

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FIGURE 48

AACAAAGTTCAGTGACTGAGAGGGCTGAGCGGAGGCTGCTGAAGGGGAGAAAGGAGTGAGGA
GCTGCTGGGCAGAGAGGGACTGTCCGGCTCCCAGATGCTGGGCCTCCTGGGGAGCACAGCCC
TCGTGGGATGGATCACAGGTGCTGCTGTGGCGGTCTGCTGCTGCTGCTGCTGCTGGCCACC
TGCCCTTTTCCACGGACGGCAGGACTGTGACGTGGAGAGGAACCGTACAGCTGCAGGGGAAA
CCGAGTCCGCCGGGCCCCAGCCTTGCCCTTCCGGCGGCGGGCCACCTGGGAATCTTTCACC
ATCACCGTCATCCTGGCCACGTATCTCATGTGCCGAATGTGGGCCTCCACCACCACCACCAC
CCCCGCCACACCCCTCACCACCTCCACCACCACCACCACCCCCACCGCCACCATCCCCGCCA
CGCTCGCTTGAGGCTGCTGTGCGCCGGTGCCCTGTGGACAGCAGCTGCCCCCTGCCCTCCCATCTG
TTCCCAGGACAAGTGGACCCCATGTTTCCATGTGGAAGGATGCATCTCTGGGGTGAACGAGG
GGAACAATAGACTGGGGCTTGCTCCAGCTGCATTTGCATGGCATGCCCCAGTGTACTATGGC
AGCAGAGAATGGAGGAACACTGGGTCTGCAGTGCTGAAGGGTTTGGGGAGTGGAGAGCAAGG
GTGCTCTTTCGGGGCTGGACAGCCCGTCTTGTGACAGTGAAGTCCCAGTGAGCCCCAGAAATG
ACAAGCGTGCTTGGCAGAGCCAGCACACAAGTGGATGTGAAGTGCCCGTCTTGACCTCCTC
ATCAGGCTGCTGCAGGCCTCTGGCGGGCAGGGCACTGGGAGAGGCCCTGAGAATGTCCTTTT
GGTTTGGAGAAGGCAGTGTGAGGCTGCACAGTCAATTTCATCGGTGCCTTAGTCCAAGAAAAT
AAAAACCACTAAGAAGCTTTAAAAAAAAAAAAAAAAAAAAA

FIGURE 49

MLGLLGSTALVGWITGAAVAVLLLLLLLLLATCLFHGRQDCDVERNRTAAGGNRVRRAPWPFR
RRGHLGIFHHHRHPGHVSHVFPNVGLHHHHHPRHTPHHLHHHHHPHRHHPRHAR

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FIGURE 50

GGCGGCTGCTGAGCTGCCTTGAGGTGCAGTGTTGGGGATCCAGAGCCATGTCGGACCTGCTA
CTACTGGGCCTGATTGGGGGCCTGACTCTCTTACTGCTGCTGACGCTGCTGGCCTTTTGCCGG
GTACTCAGGGCTACTGGCTGGGGTGGAAGTGAGTGCTGGGTACCCCCCATCCGCAACGTCA
CTGTGGCCTACAAGTTCCACATGGGGCTCTATGGTGAGACTGGGCGGCTTTTCACTGAGAGC
TGCAGCATCTCTCCCAAGCTCCGCTCCATCGCTGTCTACTATGACAACCCCCACATGGTGCC
CCCTGATAAGTGCCGATGTGCCGTGGGCAGCATCCTGAGTGAAGGTGAGGAATCGCCCTCCC
CTGAGCTCATCGACCTCTACCAGAAATTTGGCTTCAAGGTGTTCTCCTTCCCGGCACCCAGC
CATGTGGTGACAGCCACCTTCCCCTACACCACCATTTCTGTCCATCTGGCTGGCTACCCGCCG
TGTCCATCCTGCCTTGGACACCTACATCAAGGAGCGGAAGCTGTGTGCCTATCCTCGGCTGG
AGATCTACCAGGAAGACCAGATCCATTTTCATGTGCCCCACTGGCACGGCAGGGAGACTTCTAT
GTGCCCTGAGATGAAGGAGACAGAGTGGAATGGCGGGGGCTTGTGGAGGCCATTGACACCCA
GGTGATGGCACAGGAGCTGACACAATGAGTGACACGAGTTCTGTAAGCTTGGAAAGTGAGCC
CTGGCAGCCGGGAGACTTCAGCTGCCACACTGTACCTGGGGCGAGCAGCCGTGGCTGGGAT
GACGGTGACACCCGCGAGCGAGCACAGCTACAGCGAGTCAGGTGCCAGCGGCTCCTCTTTTGA
GGAGCTGGACTTGGAGGGCGAGGGGCCCTTAGGGGAGTCACGGCTGGACCTGGGACTGAGC
CCCTGGGGACTACCAAGTGGCTCTGGGAGCCCACTGCCCCCTGAGAAGGGCAAGGAGTAACCC
ATGGCCTGCACCCCTCCTGCAGTGCAGTTGCTGAGGAACTGAGCAGACTCTCCAGCAGACTCT
CCAGCCCTCTTCCTCCTTCTCTGGGGGAGGAGGGGTTCTGAGGGACCTGACTTCCCCTGC
TCCAGGCCTCTTGCTAAGCCTTCTCCTCACTGCCCTTTAGGCTCCCAGGGCCAGAGGAGCCA
GGGACTATTTTCTGCACCAGCCCCCAGGGCTGCCGCCCTGTTGTGTCTTTTTTTTTCAGACTC
ACAGTGGAGCTTCCAGGACCCAGAATAAAGCCAATGATTTACTTGTTTCACCTGGAAAAAAA
AAAAAAAAA

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FIGURE 51

MSDLLLLGLIGGLTLLLLLTLLAFAGYSGLLAGVEVSAGSPPIRNVTVAYKFHMGLYGETGR
LFTESCSISPKLRSIAVYYDNPHMVPPDKCRCVGSILSEGEESPSPELIDLYQKFGFKVFS
FPAPSHVVTATFPYTTILSIWLATRRVHPALDTYIKERKLCAYPRLEIYQEDQIHFMCPAR
QGDFYVPEMKETEWKWRGLVEAIDTQVDGTGADTMSDTSSVSLEVSPGSRETSAAATLSPGAS
SRGWDDGDTRSEHSYSESGASGSSFEELDLEGEGLGESRLDPGTEPLGTTKWLWEPTAPEKGKE

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FIGURE 52

CCGCGGGAACGCTGTCCTGGCTGCCGCCACCCGAACAGCCTGTCCTGGTGCCCCGGCTCCCT
GCCCCGCGCCAGTCATGACCCTGCGCCCCCTCACTCCTCCCGCTCCATCTGCTGCTGCTGCT
GCTGCTCAGTGCGGCGGTGTGCCGGGCTGAGGCTGGGCTCGAAACCGAAAGTCCCGTCCGGA
CCCTCCAAGTGGAGACCCTGGTGGAGCCCCCAGAACCATGTGCCGAGCCCGCTGCTTTTGA
GACACGCTTCACATACACTACACGGAAGCTTGGTAGATGGACGTATTATTGACACCTCCCT
GACCAGAGACCCTCTGGTTATAGAACTTGGCCAAAAGCAGGTGATTCCAGGTCTGGAGCAGA
GTCTTCTCGACATGTGTGTGGGAGAGAAGCGAAGGGCAATCATTCCTTCTCACTTGGCCTAT
GGAAAACGGGGATTTCCACCATCTGTCCCAGCGGATGCAGTGGTGCAGTATGACGTGGAGCT
GATTGCACTAATCCGAGCCAACTACTGGCTAAAGCTGGTGAAGGGCATTTCCTCTGGTAG
GGATGGCCATGGTGCCAGCCCTCCTGGGCCTCATTGGGTATCACCTATACAGAAAGGCCAAT
AGACCCAAAGTCTCCAAAAGAAGCTCAAGGAAGAGAAACGAAACAAGAGCAAAAAGAATA
ATAAATAATAAATTTTAAAAAACTTAAAAAAAAAAAAAAAAAAAA

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FIGURE 53

MTLRPSILPLHLGLLLLLLSAAVCGRAEAGLETESPVRTLOVETLVEPPERCAEPAAFGDTLHI
HYTGSLVDGRIIDTSLTRDPLVIELGQKQVIPGLEQSLLDMCVGEKRRAIIPSHLAYGKRGF
PPSVPADAVVQYDVELIALIRANYWLKLVKGILPLVGMAMVPALLGLIGYHLYRKANRPKVS
KKKLKEEKRNKSKKK

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FIGURE 54

CCCGGGAACGTGTTCCCTGGCTGCCGCACCCGAACAGCCTGTCCTGGTGCCCCGGCTCCCTGC
CCCGCGCCCAAGTCATGACCCTGCGCCCCCTCACTCCTCCCGCTCCATCTGCTGCTGCTGCTGC
TGCTCAGTGCGGCGGTGTGCCGGGCTGAGGCTGGGCTCGAAACCGAAAGTCCCGTCCGGACC
CTCCAAGTGAGACCCCTGGTGGAGCCCCCAGAACCATGTGCCGAGCCCGCTGCTTTTGGAGA
CACGCTTCACATACACTACACGGGAAGCTTGGTAGATGGACGTATTATTGACACCTCCCTGA
CCAGAGACCCCTCTGGTTATAGAAGCTTGGCCAAAAGCAGGTGATTCCAGGTCTGGAGCAGAGT
CTTCTCGACATGTGTGTGGGAGAGAAGCGAAGGGCAATCATTCCTTCTCACTTGGCCTATGG
AAAACGGGGATTTCCACCATCTGTCCCAGCGGATGCAGTGGTGCAGTATGACGTGGAGCTGA
TTGCACTAATCCGAGCCAACTACTGGCTAAAAGCTGGTGAAGGGCATTTTGCCTCTGGTAGGG
ATGGCCATGGTGCCACCCTCCTGGGCCTCATTTGGGTATCACCTATACAGAAAGGCCAATAGA
CCCAAAGTCTCCAAAAAGAAAGCTCAAGGAAGAGAAACGAAACAAGAGCAAAAAGAAATAATA
AATAATAAATTTTAAAAAACTTA

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FIGURE 55

CCGAAAGTCCCGTCCGGACCCTCCAAGTGGAGACCCTGGTGGAGCCCCCAGAACCATGTGCC
GAGCCCGCTGCTTTTGGAGACACGCTTCACATACACTACACGGGAAGCTTGGTAGATGGACG
TATTATTGACACCTCCCTGACCAGAGACCCTCTGGTTATAGAACTTGGCCAAAAGCAGGTGA
TTCCAGGTCTGGAGCAGAGTCTTCTCGACATGTGTGTGGGAGAGAAGCGAAGGGCAATCATT
CCTTCTCACTTGGCCTATGGAAAACGGGGATTTCCACCATCTGTCCCAGCGGATGCAGTGGT
GCAGTATGACGTGGAGCTGATTGCACTAATCCGAGCCAACACTGGCTAAAGCTGGTGAAGG
GCATTTTGCCCTCTGGTAGGGATGGCCATGGTGCCAGCCCTCCTGGGCCTCATTGGGTATCAC
CTATACAGAAAGGCCAATAGACCCAAAGTCTCCAAAAAGAAGCTCAAGGAAGAGAAACGAAA
CAAGAGCAAAAAGAAATAATAAATAATAAATTTTAAAAAACTTAAAA

CTGCTGCATCCGGGTGCTCTGGAGGCTGTGGCCGTTTTGTTTTCTTGGCTAAAAATCGGGGGAG
TGAGGCGGGCCGGCGCGGCGCACACCGGGCTCCGGAACCACTGCACGACGGGGCTGGACTG
ACCTGAAAAAAATGCTCTGGATTTCTAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGG
GAAAAGCGCAATACTATTGCTTCCATTGCTGCTGGTGTACTATTTTTTACAGGCTGGTGGAT
TATCATAGATGCAGCTGTTATTTATCCCACCATGAAAGATTTC AACCACTCATACCATGCCT
GTGGTGTTATAGCAACCATAGCCTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGA
GGTGATAGTTACAGTGAAGGTTGTCTGGGTCAAACAGGTGCTCGCATTTGGCTTTTCGTTGG
TTTCATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGGATTCTTTTTGGAGGTTATGTTG
CTAAAGAAAAAGACATAGTATACCCTGGAATTGCTGTATTTTTCCAGAATGCCTTCATCTTT
TTTGGAGGGCTGGTTTTTAAAGTTTGGCCGCACTGAAGACTTATGGCAGTGAACACATCTGAT
TTCCACAGCACAACAGCCCTGCATGGGTTTGTGTTGTTTTTTTACTGCTCACTCCCAACCTT
TTGTAATGCCATTTTCTAAACTTATTTCTGAGTGTAGTCTCAGCTTAAAGTTGTGTAATACT
AAAATCACGAGAACACCTAAACAACAACCAAAAATCTATTGTGGTATGCATTGATTAACTT
ATAAAATGTTAGAGGAACTTTACATGAATAATTTTTGTCAAATTTTATCATGGTATAATT
TGTA AAAAATAAAAAGAAATTACAAAAGAAATTATGGATTGTCAATGTAAGTATTTGTCATA
TCTGAGGTCCAAAACCACAATGAAAGTGCTCTGAAGATTTAATGTGTTTATTCAAATGTGGT
CTCTTCTGTGTCAAATGTTAAATGAAATATAAACATTTTTTAGTTTTTAAATATTCCGTGG
TCAAAATTCTTCCTCACTATAATTGGTATTTACTTTTACCAAAAATTCTGTGAACATGTAAT
GTA ACTGGCTTTTGGAGGTCTCCAAGGGGTGAGTGGACGTGTTGGAAGAGAGAAGCACCAT
GGTCCAGCCACCAGGCTCCCTGTGTCCCTTCCATGGGAAGGTCTTCCGCTGTGCCTCTCATT
CCAAGGGCAGGAAGATGTGACTCAGCCATGACACGTGGTCTGGTGGGATGCACAGTCACTC
CACATCCACCACTG

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FIGURE 57

MSGFLEGLRCSECIDWGEKRNTIASIAAGVLFFGWIIIDA AVIYPTMKDFNHSYHACGVI
ATIAFLMINAVSNGQVRGDSYSEGCLGQTGARIWLFVGFMLAFGSLIASMWILFGGYVAKEK
DIVYPGIAVFFQNAFIFFGGLVFKFGRTEDLWQ

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FIGURE 58

TTCTTGGCTAAAATCGGGGGAGTGAGGCGGGCCGGCGCGGCGACACCGGGCTCCGGAACC
ACTGCACGACGGGGCTGGACTGACCTGAAAAAATGTCTGGATTTCTAGAGGGCTTGAGATG
CTCAGAATGCATTGACTGGGGGGAAAAGCGCAATACTATTGCTTCCATTGCTGCTGGTGTAC
TATTTTTTACAGGCTGGTGGATTATCATAGATGCAGCTGTTATTTATCCCACCATGAAAGAT
TTCAACCACTCATACCATGCCTGTGGTGTATAGCAACCATAGCCTTCCTAATGATTAATGC
AGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTTGTCTGGGTCAAACAGGTG
CTCGCATTTGGCTTTTCGTTGGTTTCATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGG
ATTCTTTTTTGGAGGTTATGTTGCTAAAGAAAAAGACATAGTATACCCTGGAATTGCTGTATT
TTTCCAGAATGCCTTCATCTTTTTTGGAGGGCTGGTTTTTAAGTTTGGC

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FIGURE 59

TGGACGGACCTGAAAAAATGTTTGGATTNTAGAGGGNTTGAGATGTTCAGAATGCATGAC
TGGGGGAAAAGCGCAAATACTATTGCTTCCATTGCTGCTGGTGTANTATTTTTTACAGGCTG
GTGGATTATCATAGATGCAGNTGTTATTTATCCCACCATGAAAGATTTCAACCANTCATACC
ATGCCTGTGGTGTTATAGCAACCATAGCCTTCNTAATGATTAATGCAGTATCGAATGGACAA
GTCCGAGGTGATAGTTACAGTGAAGGTTGTTTGGGTCAAACAGGTGCTCGCATTGCGCTTTT
CGTTGGTTTCATGTTGGCCTTTGGATCTCTGATTGCATCTATGTGGATTCTTTTTGGAGGTT
ATGTTGCTAAAGAAAAAGACATAGTATACCCTGGAATTGNTGTATTTTTCCAGAATGCCTTC
ATCTTTTTTGGAGGGCTGGTTTTTAAGTTTGGCCGCACTGAAGANTTATGGCAGTG

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FIGURE 60

GGACACGGGGTTCCGGACCAATGCANGACGGGGTGGANTGACCTGAAAAAATGTTTGGATT
TTTAGAGGGCTTGAGATGNTCAGAATGCATTGACTGGGGGAAAAGCGCAATANTATTGCTTT
CCATTGCTGCTGGTGTACTATTTTTTACAGGGTGGTGGATTATCATAGATGCAGCTGTTATT
TATCCCACCATGAAAGATTTNAACCACTCATACCATGCCTGTGGTGTTATAGCAACCATAGC
CTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTT
GTTTGGGTCAAACAGGTGNTCGCATTTGGCTTTTCGTTGGTTTCATGTTGGCCTTTGGATTT
CTGATTGNATTCTATGCGGATTCTTCTTGGAGGTTATGTTGCTAAAGAAAAAGACATAGTAT
ACCCTGGAATTNCTNTATTTTTCCAGAATGCC

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FIGURE 61

TAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGGGAAAAGCGCAATANTATTGCTTCC
ATTGNTGNTGGTGTANTATTTTTTTACAGGCTGGTGGATTATNATAGATGCAGCTGTTATTT
ATCCCACCATGAAAGATTTNAACCANTCATACCATGCCTGTGGTGTTATAGCAACCATAGCC
TTCCTAATGATTAATGCAGTATNGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTTG
TTTGGGTCAAACAGGTGNTNGCATTGGCTTTTNGTTGGTTTCATGTTGGCCTTTGGATCTN
TGATTGCATTTATGTGGATTNTTTTTGGAGGTTATGTTGCTAAAGNAAAAGACATAGTATAC
CCTGT

FIGURE 62

GGGAGGCTGTGNCCGTTTTGTTTTN.TGGCTAAAATCGGGGGAGTGAGGCGGCCCGGCGCGG
CGNGACACCGGGTTCCGGGAACCATTCACGACGGGGTGGACTGACCTGAAAAAATGTTTG
GATTNTAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGGGAAAAGCGCAATACTATT
GCTTCCATTGCTGCTGGTGTAATAATTTTACAGGCTGGTGGATTATCATAGATGCAGCTGT
TATTTATCCCACCATGAAAGATTTCAACCACTCATACCATGCCTGTGGTGTATAGCAACCA
TAGCCTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAA
GGTTGTCTGGGTCAAACAGGTGCTCGCAATTTGGCTTTTCGTTGGTTTCATGTTGGCCTTTGG
ATNTCTGATTGCATCTATGTGGATTCTTTTTGGAGGTTATGTTGCTAAAGAAAAAGACATAG
TATACCTGGAATTGCTGTATTTTTCCAGAATGCCTTCATNTTTTTTGGAGGGCTG

FIGURE 63

CGACGCCGGCGTGATGTGGCTTCCGCTGGTGTCTCCTGGCTGTGCTGCTGCTGGCCGTCC
TCTGCAAAGTTTACTTGGGACTATTCTCTGGCAGCTCCCCGAATCCTTTCTCCGAAGATGTC
AAACGGCCCCCAGCGCCCTGGTAAGTACAAGGAGGCCAGGAAGAAGGTTCTCAAAACAAGC
TTTTTTCAGCCAACCAAGTGCCGAGAAGCTGGATGTGGTGGTAATTGGCAGTGGCTTTGGGG
GCCTGGCTGCAGCTGCAATTCTAGCTAAAGCTGGCAAGCGAGTCTGGTGTGGAACAACAT
ACCAAGGCAGGGGGCTGCTGTACATCCTTTGGAAAGAATGGCCTTGAATTTGACACAGGAAT
CCATTACATTGGGCGTATGGAAGAGGGCAGCATTGGCCGTTTTATCTTGGACCAGATCACTG
AAGGGCAGCTGGACTGGGCTCCCCTGTCTCTCCTTTTGACATCATGGTACTGGAAGGGCCC
AATGGCCGAAAGGAGTACCCCATGTACAGTGGAGAGAAAGCCTACATTACAGGGCCTCAAGGA
GAAGTTTCCACAGGAGGAAGCTATCATTGACAAGTATATAAAGCTGGTTAAGGTGGTATCCA
GTGGAGCCCCCTCATGCCATCCTGTTGAAATTCCTCCCATTGCCCCGTGGTTTCAGCTCCTCGAC
AGGTGTGGGCTGCTGACTCGTTTTCTCTCCATTCTTCAAGCATCCACCCAGAGCCTGGCTGA
GGTCTCTGCAGCAGCTGGGGGCCTCCTCTGAGCTCCAGGCAGTACTCAGCTACATCTTCCCCA
CTTACGGTGTCACCCCAACCAACAGTGCCTTTTTCATGCACGCCCTGCTGGTCAACCACTAC
ATGAAAGGAGGCTTTTATCCCCGAGGGGGTTCCAGTGAAATTGCCTTCCACACCATCCCTGT
GATTACAGCGGGCTGGGGGCGCTGTCTCACAAGGCCACTGTGCAGAGTGTGTTGCTGGACT
CAGCTGGGAAAGCCTGTGGTGTGAGTGTGAAGAAGGGGCATGAGCTGGTGAACATCTATTGC
CCCATCGTGGTCTCCAACGCAGGACTGTTCAACACCTATGAACACCTACTGCCGGGGAACGC
CCGCTGCCTGCCAGGTGTGAAGCAGCAACTGGGGACGGTGCGGCCCGGCTTAGGCATGACCT
CTGTTTTTCATCTGCTGCGAGGCACCAAGGAAGACCTGCATCTGCCGTCCACCAACTACTAT
GTTTACTATGACACGGACATGGACCAGGCGATGGAGCGCTACGTCTCCATGCCAGGGAAGA
GGCTGCGGAACACATCCCTCTTCTCTTCTGCTTTCCCATCAGCCAAAGATCCGACCTGGG
AGGACCGATTCCCAGGCCGGTCCACCATGATCATGCTCATACCCACTGCCTACGAGTGGTTT
GAGGAGTGGCAGGCGGAGCTGAAGGGAAAGCGGGCAGTGACTATGAGACCTTCAAAAACCTC
CTTTGTGGAAGCCTCTATGTGAGTGGTCTCTGAAACTGTTCCACAGCTGGAGGGGAAGGTGG
AGAGTGTGACTGCAGGATCCCCACTCACCACAGTTCTATCTGGCTGCTCCCCAGGTGCC
TGCTACGGGGCTGACCATGACCTGGGCCGCTGCACCTTGTGTGATGGCCTCCTTGAGGGC
CCAGAGCCCCATCCCCAACCTCTATCTGACAGGCCAGGATATCTTACCTGTGGACTGGTCTG
GGGCCCTGCAAGGTGCCCTGCTGTGCAGCAGCGCCATCCTGAAGCGGAACCTTGTAAGTCA
CTTAAGAATCTTGATTCTAGGATCCGGGCACAGAAGAAAAAGAATTAGTTCCATCAGGGAGG
AGTCAGAGGAATTTGCCCAATGGCTGGGGCATCTCCCTTGACTTACCCATAATGTCTTTCTG
CATTAGTTCCCTTGACGTATAAAGCACTCTAATTTGGTTCTGATGCCTGAAGAGAGGCCTAG
TTTAAATCACAATCCGAATCTGGGGCAATGGAATCACTGCTTCCAGCTGGGGCAGGTGAGA
TCTTTACGCCCTTTTATAACATGCCATCCCTACTAATAGGATATTGACTTGGATAGCTTGATG
TCTCATGACGAGCGGCGCTCTGCATCCCTCACCCTGCCTCCTAACTCAGTGATCAAAGCGA
ATATTCCATCTGTGGATAGAACCCTGGCAGTGTGTGAGCTCAACCTGGTGGGTTCAAGTTC
TGTCTGAGGCTTCTGCTCTCATTCAATTTAGTGCTACGCTGCACAGTTCTACACTGTCAAGG
GAAAAGGGAGACTAATGAGGCTTAACTCAAAACCTGGGCGTGGTTTTGGTTGCCATTCCATA
GGTTTGGAGAGCTCTAGATCTCTTTTGTGCTGGGTTCAAGTGGCTCTTACAGGGACAGGAAT
GCCTGTGTCTGGCCAGTGTGGTTCTGGAGCTTTGGGGTAACAGCAGGATCCATCAGTTAGTA
GGGTGCATGTGAGATGATCATATCCAATTCATATGGAAGTCCCGGGTCTGTCTCTCTTATCA
TCGGGGTGGCAGCTGGTTCTCAATGTGCCAGCAGGACTCAGTACCTGAGCCTCAATCAAGC
CTTATCCACCAAATACACAGGGAAGGGTGATGCAGGGAAGGGTGACATCAGGAGTCAGGGCA
TGGACTGGTAAGATGAATACTTTGCTGGGCTGAAGCAGGCTGCAGGGCATTCCAGCCAAGGG
CACAGCAGGGGACAGTGCAGGGAGGTGTGGGGTAAGGGAGGGGAAGTCACATCAGAAAAGGGA
AAGCCACGGAATGTGTGTGAAGCCAGAAATGGCATTGTCAGTTAATTAGCACATGTGAGGG
TTAGACAGGTAGGTGAATGCAAGCTCAAGGTTTGGAAAAATGACTTTTTCAGTTATGTCTTTG
GTATCAGACATACGAAAGGTCTCTTTGTAGTTCTGTGTTAATGTAAACATTAATAAATTTATTG
ATTCCATTGCTTTAAAAA

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FIGURE 64

MWLPLVLLLAVALLLAVLCKVYLGLFSGSSPNPFSSEVVRPPAPLVTDKEARKKVLKQAFSAN
QVPEKLDVVVIGSGFGGLAAAAILAKAGKRVLVLEQHTKAGGCCHTFGKNGLEFDTGIHYIG
RMEEGSIGRFILDQITEGQLDWAPLSSPFDIMVLEGPNRKEYPMYSGEKAYIQGLKEKFPQ
EEAIIIDKYIKLVKVVSSGAPHAILLKFLPLPVVQLLDRCGLLTRFSPFLQASTQSLAEVLQQ
LGASSELQAVLSYIFPTYGVTPNHSAFSMHALLVNHYMKGGFYPRGGSSEIAFHTIPVIQRA
GGAVLTKATVQSVLLDSAGKACGVSVKKGHELVNIYCPVVSNAGLFNTYEHLLPGNARCLP
GVKQQLGTVRPGGMTSVFICLRGTKEDLHLPSTNYYVYYDTMDQAMERYVSMFREEAAEH
IPLLFFAFPSAKDPTWEDRFPGRSTMIMLIPTAYEWFEWQAELKGKRGSDYETFKNSFVEA
SMSVVLKLFPPQLEGKVESVTAGSPLTNQFYLAAPRGACYGADHDLGRLHPCVMASLRAQSPI
PNLYLTGQDIFTGCLVGALQGALLCSSAILKRNLYSDLKNLDSRIRAQKKKN

[illegible]

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FIGURE 66

MRVRIGLTLLLCVLLSLASASSDEEGSQDESLDSKTTLTSDSVKDHTTAGRVVAGQIFLD
SESELESSIQEEEDSLK3QEGESVTEDISFLESPNPENKDYEEPKKVRKPALTAIEGTAHG
EPCHFPPFLFLDKEYDECTSDGREDGRLWCATTYDYKADEKWGFCETEEEEAAKRRQMQAEMM
YQTGMKILNGSNKKSQKREAYRYLQKAASMNHTKALERVSYALLFGDYLPQNIQAAREMF EK
LTEEGSPKGQTALGFLYASGLGVNSSQAKALVYYTFGALGGNLI AHMVLVSRL

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FIGURE 67

CTTCCCAGCCCTGTGCCCCAAAGCACCTGGAGCATATAGCCTTGCAGAACTTCTACTTGCCT
GCCTCCCTGCCTCTGGCCATGGCCTGCCGGTGCCTCAGCTTCCTTCTGATGGGGACCTTCCT
GTCAGTTTCCCAGACAGTCCTGGCCCAGCTGGATGCACTGCTGGTCTTCCCAGGCCAAGTGG
CTCAACTCTCCTGCACGCTCAGCCCCCAGCACGTCAACATCAGGGACTACGGTGTGTCTCTGG
TACCAGCAGCGGGCAGGCAGTGCCCCCTCGATATCTCCTCTACTACCGCTCGGAGGAGGATCA
CCACCGGCCTGCTGACATCCCCGATCGATTCTCGGCAGCCAAGGATGAGGCCCACAATGCCT
GTGTCTCACCATTAGTCCCGTGCAGCCTGAAGACGACGCGGATTACTACTGCTCTGTTGGC
TACGGCTTTAGTCCCTAGGGGTGGGGTGTGAGATGGGTGCCTCCCCTCTGCCTCCCATTTCT
GCCCCTGACCTTGGGTCCCTTTTAACTTTCTCTGAGCCTTGCTTCCCCTCTGTAAAATGGG
TTAATAATATTCAACATGTCAACAAC

FIGURE 68

MACRCLSFLMGTFLSVSQTVLAQLDALLVFPQVAQLSCTLSPQHVTIRDYGVSWYQQRAG
SAPRYLLYYRSEEDHHRPADIPDRFSAKDEAHNACVLTISPVQPEDDADYYCSVGYGFS

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FIGURE 69

GCCGCCCCGCCCCGAGACCGGGCCCCGGGGCGCGGGGCGCGGGATGCGGCGCCCCGGGGCGG
CGATGACCGCGGAGCGCACGCCGCGGGCCCCGCCCTGACCCCGCGCCCGCCCGCTGAGCCC
CCCCCGGAGGTCCGGACAGGCCGAGATGACGCCGAGCCCCCTGTTGCTGCTCCTGCTGCCGC
CGCTGCTGCTGGGGGCTTCCACCCGGCCGCGCCGCGCCGAGGCCCCCAAAGATGGCGGAC
AAGGTGGTCCACGGCAGGTGGCCCGGCTGGGCCGCACTGTGCGGCTGCAGTGCCCACTGGA
GGGGGACCCCGCCCGCTGACCATGTGGACCAAGGATGGCCGACCATCCACAGCGGCTGGA
GCCGCTTCCGCGTGCTGCCGAGGGGCTGAAGGTGAAGCAGGTGGAGCGGGAGGATGCCGGC
GTGTACGTGTGCAAGGCCACCAACGGCTTCGGCAGCGCTGAGCGTCAACTACACCTTCGTCTG
GCTGGATGACATTAGCCAGGGAAGGAGAGCCTGGGGCCCGACAGCTCCTCTGGGGGTCAAG
AGGACCCCGCCAGCCAGCAGTGGGCACGACCGCGCTTCACACAGCCCTCCAAGATGAGGCGC
CGGGTGATCGCACGGCCCGTGGGTAGCTCCGTGCGGCTCAAGTGCGTGCCAGCGGGCACCC
TCGGCCCGACATCAGTGGATGAAGGACGACAGGCCCTTGACGCGCCAGAGGCCGCTGAGC
CCAGGAAGAAGAAGTGGACACTGAGCCTGAAGAACCTGCGGCCGAGGACAGCGGCAAAATAC
ACCTGCCGCGTGTCGAACCGCGCGGGCGCCATCAACGCCACCTACAAGGTGGATGTGATCCA
GCGGACCCCGTCCAAGCCCCGTGCTCACAGGCACGCAACCCGTGAACACGACGCTGACTTCG
GGGGGACCACGTCTCTCCAGTGCAAGGTGCGCAGCGACGTGAAGCCGGTGATCCAGTGGCTG
AAGCGCGTGGAGTACGGCGCCGAGGGCCGCCAACCTCCACCATCGATGTGGGCGCCAGAA
GTTTGTGGTGCTGCCACGGGTGACGTGTGGTCCGCGCCGACGGCTCCTACCTCAATAAGC
TGCTCATACCCGTGCCCGCCAGGACGATGCGGGCATGTACATCTGCCCTTGGCGCCAACACC
ATGGGCTACAGCTTCCGACGCGCCTTCCCTACCGTGCTGCCAGACCCAAAACCGCCAGGGCC
ACCTGTGGCCTCCTCGTCTCGGCCACTAGCCTGCCGTGGCCCGTGGTTCATCGGCATCCAG
CCGGCGCTGTCTTCATCTTGGGCACCCCTGCTCCTGTGGCTTTGCCAGGCCCAGAAGAAGCCG
TGACCCCCCGCGCTGCCCTTCCCTGCTGGGCACCGCCCGCCGGGGACGGCCCCGCGACCG
CAGCGGAGACAAGGACCTTCCCTCGTTGGCCGCCCTCAGCGCTGGCCCTGGTGTGGGGCTGT
GTGAGGAGCATGGGTCTCCGGCAGCCCCCAGCACTTACTGGGCCCAGGCCAGTTGCTGGC
CCTAAGTTGTACCCCAAACCTCTACACAGACATCCACACACACACACACACACTCTACAC
ACACTCACACGTGGAGGGCAAGGTCCACCAGCACATCCACTATCAGTGCTAGACGGCACCGT
ATCTGCAGTGGGCACGGGGGGGCCCGCCAGACAGGCAGACTGGGAGGATGGAGGACGGAGCT
GCAGACGAAGGCAGGGGACCCATGGCGAGGAGGAATGGCCAGCACCCCAAGGCAGTCTGTGTG
TGAGGCATAGCCCTGGACACACACACACAGACACACACTACCTGGATGCATGTATGCAC
ACACATGCGCGCACACGTGCTCCCTGAAGGCACACGTACGCACACGCACATGCACAGATATG
CCGCCTGGGCACACAGATAAGCTGCCCAAATGCACGCACACGCACAGAGACATGCCAGAACA
TACAAGGACATGCTGCCTGAACATACACACGCACACCCATGCGCAGATGTGTCTGGACA
CACACACACACACGGATATGCTGTCTGGACGCACACACGTGCAGATATGGTATCCGGACACA
CACGTGCACAGATATGCTGCCTGGACACACAGATAATGCTGCCTTGACACACACATGCACGG
ATATTGCCCTGGACACACACACACACACACGCGTGACAGATATGCTGTCTGGACACGCACAC
ACATGCAGATATGCTGCCTGGACACACACTTCCAGACACACGTGCACAGGCGCAGATATGCT
GCCTGGACACACGCAGATATGCTGTCTAGTCACACACACACGCAGACATGCTGTCCGGACAC
ACACACGCATGCACAGATATGCTGTCCGGACACACACACGCACGCAGATATGCTGCCTGGAC
ACACACACAGATAATGCTGCCTCAACACTCACACACGTGCAGATATTGCCTGGACACACACA
TGTGCACAGATATGCTGTCTGGACATGCACACACGTGCAGATATGCTGTCCGGATACACACG
CACGCACACATGCAGATATGCTGCCTGGGCACACACTTCCGGACACACATGCACACACAGGT
GCAGATATGCTGCCTGGACACACACACAGATAATGCTGCCTCAACACTCACACACGTGCAGA
TATTGCCTGGACACACACATGTGCACAGATATGCTGTCTGGACATGCACACACGTGCAGATA
TGCTGTCCGGATACACACGCACGCACACATGCAGATATGCTGCCTGGGCACACACTTCCGGA
CACACATGCACACACAGGTGCAGATATGCTGCCTGGACACACGCAGACTGACGTGCTTTTGG
GAGGGTGTGCCGTGAAGCCTGCAGTACGTGTGCCGTGAGGCTCATAGTTGATGAGGGACTTT
CCCTGCTCCACCGTCACTCCCCAACTCTGCCCGCCTCTGTCCCCGCCTCAGTCCCCGCCTC
CATCCCCGCTCTGTCCCCTGGCCTTGGCGGCTATTTTTGCCACCTGCCCTTGGGTGCCCAGG
AGTCCCCTACTGCTGTGGGCTGGGGTGGGGGACAGCAGCCCCAAGCCTGAGAGGCTGGAG
CCCATGGCTAGTGGCTCATCCCCAGTGCACTTCTCCCCCTGACACAGAGAAGGGGCCCTGGTA
TTTATATTTAAGAAATGAAGATAATTAATAATGATGGAAGGAAGACTGGGTGTCAGGGAC
TGTGGTCTCTCTGGGGCCCGGGACCCGCTGGTCTTTCAGCCATGCTGATGACCACACCCC
GTCCAGGCCAGACACCACCCCCACCCCACTGTCTGGTGGCCCCAGATCTCTGTAATTTTA
TGTAGAGTTTGTAGCTGAAGCCCCGTATATTTAATTTATTTTGTAAACACAAAA

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FIGURE 70

MTPSPLLLLLLPPLLLGAFPPAAAARGPPKMADKVVPRQVARLGRTVRLQCPVEGDPPPLTM
WTKDGRTIHSGWSRFRVLPQGLKVKQVEREDAGVYVCKATNGFGSLSVNYTLVVLLDDISPGK
ESLGPDSSSSGGQEDPASQQWARPRFTQPSKMRRRVIA RPVGSSVRLKCVASGHRPDITWMK
DDQALTRPEAAEPRKKKWTLSLKNLRPEDSGKYTCRVSNRAGAINATYKVDVIQRTRSKPVL
TGTHPVNTTVDFGGTTSFQCKVRSDVKPVIQWLKRVEYGAEGRHNSTIDVGGQKFVVLPTGD
VWSRPDGSYLNKLLITRARQDDAGMYICLGANTMGYSFRSAFLT VLPDPKPPGPPVASSSSA
TSLPWPVVIGIPAGAVFILGTLLLWLCQAQKKPCTPAPAPPLPGHRPPGTARDRSGDKDLPS
LAALSAGPGVGLCEEHGSPAAPQHLLGPGPVAGPKLYPKLYTDIHTHTHTSHHTSHSHVEGKV
HQHIHYQC

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FIGURE 71A

CCCAGCTGAGGAGCCCTGCTCAAGACACGGTCACTGGATCTGAGAACTTCCCAGGGGACCG
 CATTCC?GAGTCAGTGACTCTGTGAAGCACCCACATCTACCTCTTGCCACGTTCCCACGGGC
 TTGGGGGAAAGATGTTGGGGACCAAGCCTGGGTGTTCTCCTTCTGGTCTGGAAGTCACA
 TCTGTGTTGGGGAGACAGACGATGCTACCCAGTCAGTAAGAAGAGTCCAGCCTGGGAAGAA
 GAACCCAGCATCTTTGCCAAGCCTGCCGACACCCTGGAGAGCCCTGGTGAGTGACAAAT
 GGTTCACATCGACTACCCAGGCGGGAAGGGCGACTATGAGCGGCTGGACGCCATTTCGTTTC
 TACTATGGGGACCGTGATGTGCGCGTCCCTGCGGCTAGAGGCTCGGACCACTGTACAGCCTGT
 ACCTGCGGCAGCACTGGCCAGGTGGTCCATGGTAGTCCCCGTGAGGGTTTCTGGTGCCCTCA
 ACAGGGAGCAGCGGCCTGGCCAGAACTGCTCTAATTACACCGTACGCTTCTCTGCCACCA
 GGATCCCTGCGCCGAGACACAGAGCGCATCTGGAGCCCATGGTCTCCCTGGAGCAAGTGCTC
 AGCTGCCGTGTTGTCAGACTGGGGTCCAGACTCGCACACGCATTTGCTTGGCAGAGATGGTGT
 CGCTGTGCAGTGAGGCCAGCGAAGAGGGTCAGCACTGCATGGGCCAGGACTGTACAGCCTGT
 GACCTGACCTGCCCAATGGGCCAGGTGAATGCTGACTGTGATGCCTGCATGTGCCAGGACTT
 CATGCTTCATGGGGCTGTCTCCCTTCCCGAGGTGCCCCAGCCTCAGGGGCTGCTATCTACC
 TCCTGACCAAGACGCCGAAGCTGCTGACCCAGACAGACAGTGTGGGAGATTCCGAATCCCT
 GGCTTGTGCCCTGATGGCAAAAGCATCCTGAAGATCACAAGGTCAAGTTTGCCCCCATTTGT
 ACTCACAATGCCAAGACTAGCCTGAAGGCAGGCCACCATCAAGGCAGAGTTTGTGAGGGCAG
 AGACTCCATACATGGTGATGAACCCCTGAGACAAAAGCACGGAGAGCTGGGCAGAGCGTGTCT
 CTGTGCTGTAAGGCCACAGGGAAGCCCAGGCCAGACAAGTATTTTGGTATCATAATGACAC
 ATTGCTGGATCCTTCCCTCTACAAGCATGAGAGCAAGCTGGTGCTGAGGAACTGCAGCAGC
 ACCAGGCTGGGGAGTACTTTTGCAAGGCCAGAGTGATGCTGGGGCTGTGAAGTCCAAGGTT
 GCCCAGCTGATTGTACAGCATCTGATGAGACTCCTTGCAACCCAGTTCCTGAGAGCTATCT
 TATCCGGCTGCCCCATGATTGCTTTTCAGAATGCCACCAACTCCTTCTACTATGACGTGGGAC
 GCTGCCCTGTTAAGACTTGTGTCAGGGCAGCAGGATAATGGGATCAGGTGCCGTGATGCTGTG
 CAGAACTGCTGTGGCATCTCCAAGACAGAGGAAAGGGAGATCCAGTGCACTGGCTACACGCT
 ACCCACCAAGGTGGCCAAGGAGTGCACTGCCAGCGGTGTACGGAACTCGGAGCATCGTGC
 GGGGCCGTGTGCTGCTGCTGACAATGGGGAGCCCATGCGCTTTGGCCATGTGTACATGGGG
 AACAGCCGTGTAAGCATGACTGGCTACAAGGGCACTTTCACCTCCATGTCCCCCAGGACAC
 TGAGAGGCTGGTGCTCACATTTGTGGACAGGCTGCAGAAGTTTGTCAACACCACCAAGTGC
 TACCTTTCAACAAGAAGGGGAGTGCCGTGTTCCATGAAATCAAGATGCTTCGTGCGAAAGAG
 CCCATCACTTTTGGGAAGCCATGGAGACCAACATCATCCCCCTGGGGGAAGTGCTTGGTGAAGA
 CCCCATGGCTGAACTGGAGATTCCATCCAGGAGTTTCTACAGGCAGAATGGGGAGCCCTACA
 TAGGAAAAGTGAAGGCCAGTGTCACCTTCCCTGGATCCCCGAATATTTCCACAGCCACAGCT
 GCCCAGACTGACCTGAACTTCATCAATGACGAAGGAGACACTTTCCCCCTTCGGACGTATGG
 CATGTTCTCTGTGGACTTCAGAGATGAGTCACTCAGAGCCACTTAATGCTGGCAAAGTGA
 AGGTCCACCTTGACTCGACCCAGGTCAAGATGCCAGAGCACATATCCACAGTGAAACTCTGG
 TCACTCAATCCAGACACAGGGCTGTGGGAGGAGGAAGGTGATTTCAAATTTGAAATCAAAG
 GAGGAACAAAAGAGAAGACAGAACCTTCTGGTGGGCAACCTGGAGATTCTGTGAGAGGAGGC
 TCTTTAACCTGGATGTTCTTGAAAGCAGGCGGTGCTTTGTTAAGGTGAGGGCCTACCGGAGT
 GAGAGGTTCTTGCTTAGTGAGCAGATCCAGGGGTTGTGATCTCCGTGATTAACTGGAGCC
 TAGAATCTGGCTTCTGTGCCAACCCCTAGGGCCTGGGGCCGCTTTGACAGTGTCTACAGGCC
 CCAACGGGGCCTGTGTGCTGCTTCTGTGATGACCAGTCCCCTGATGCCTACTCTGCCTAT
 GTCTTGGCAAGCCTGGCTGGGGAGGAACTGCAAGCAGTGAGTCTTCTCTAAATTCACCCC
 AAATGCAATTGGCGTCCCTCAGCCCTATCTCAACAAGCTCAACTACCGTCGGACGGACCATG
 AGGATCCACGGGTTAAAAAAGACAGCTTTCCAGATTAGCATGGCCAAGCCAAGGCCAACTCA
 GCTGAGGAGAGCAATGGGCCCATCTATGCCCTTTGAGAACCTCCGGGCATGTGAAGAGGCACC
 ACCCAGTGACGCCACTTCCGGTTCTACCAGATTGAGGGGGATCGATATGACTACAACACAG
 TCCCCCTCAACGAAGATGACCCTATGAGCTGGACTGAAGACTATCTGGCATGGTGCCAAAAG
 CCGATGGAATTCAGGGCCTGCTATATCAAGGTGAAGATTGTGGGGCCACTGGAAGTGAATGT
 GCGATCCCGCAACATGGGGGGCACTCATCGGCGGACAGTGGGGAAAGCTGTATGGAATCCGAG
 ATGTGAGGAGCACTCGGGACAGGGACCAGCCCAATGTCTCAGCTGCCTGTCTGGAGTTCAAG
 TGCAGTGGGATGCTCTATGATCAGGACCGTGTGGACCGCACCTGGTGAAGGTCATCCCCCA
 GGGCAGCTGCCGTCGAGCCAGTGTGAACCCCATGCTGCATGAGTACCTGGTCAACCACTTGC
 CACTTGCACTCAACAACGACACCACTGAGTACACCATGCTGGCACCTTGGCACCTTGGGC
 CACAATCTAGGCATCTACACTGTCACTGACCAGGACCTCGCACGGCCAAGGAGATCGCGCT
 CGGCCGGTGTCTTGTATGGCACATCCGATGGCTCCTCCAGAATCATGAAGAGCAATGTGGGAG
 TAGCCCTCACCTTCAACTGTGTAGAGAGGCAAGTAGGCCGCCAGAGTGCTTCCAGTACCTC
 CAAAGCACCCAGCCAGTCCCTGCTGCAGGCACTGTCCAAGGAAGAGTGCCCTCGAGGAG
 GCAGCAGCGAGCGAGCAGGGGTGGCCAGCGCCAGGGTGGAGTGGTGGCCTCTCTGAGATTTT

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FIGURE 71B

CTAGAGTTGCTCAACAGCCCCTGATCAACTAAAGTTTTGTGGTACTTCACCCCTCTTCTGCCCT
CATTTCATGTGACAGCCATTGTGAGACTGATGCACAACTGTCACTTGGTTAATTTAAGCAC
TTCTGTTTTTCGTGAATTTGCTTGTGTTTTCTTCATGCCTTTACTTACTTTGTCCCATGCTA
CTGATTGGCACGTGGCCCCCACAATGGCACAATAAAAGCCCCCTTGTGAAACTGTTCTTTAAA
TGAAACACAAGAAATTGGCCACTGGTAAACTCTGCAGCTTCAACTGTACTTCATTTAATGC
CATTAATGCAAATATACTTCCTCTTCTTTTGCATGGTTTTGCCACCTCTGCAATAGTGAT
AATCTGATGCTGAAGATCAAATAACCAATATAAAGCATATTTCTTGGCCTTGCTCCACAGGA
CATAGGCAAGCCTTGATCATAGTTCATACATATAAATGGTGGTGAAATAAAGAAATAAAACA
CAATACTTTTACTTGAAATGTAAATAACTTATTTATTTCTTTGCTAAATTTGGAATTCTAGT
GCACATTCAAAGTTAAGCTATTAAATATAGGGTGATCATAGTTCCTCTACCAAGTCTGGAAA
GAACATCTCCTGGTATCCACAATTACACCAGGTTGCTAACTGTATTTGTACATTTCCTTTTG
CATTCGCTTTTGTTCCTTGCTAGAAACCCAGTGTAGCCCAGGGCAGATGTCAATAAATGCATA
CTCTGTATTTCGAAAAA

FIGURE 72

MVGTKAWVFSFLVLEVTSVLGRQTMLTQSVRRVQPGKKNPSIFAKPADTLESPGEWTTWFNI
DYPGGKGDYERLDAIRFYYGDRVCARPLRLEARTTDWTPAGSTGQVVHGSPREGFWCLNREQ
RPGQNC SNYTVRFLCPPGSLRRDTERI WSPWSPWSKCSAACGQTGVQTRTRI CLAEMVSLCS
EASEEGQHCHMGQDC TACDLT CPMGQVNADCDACMCQDFMLHGAVSLPGGAPASGAAYLLTK
TPKLLTQTDS DGRFRI PGLCPDGKSILKITKVKFAPIVLTMPKTSLKAATIKAEFVRAETPY
MVMNPETKARRAGQSVSLCCKATGKPRPDKYFWYHNDTLLDPSLYKHESKLVLRLKQLQHQA
EYFCKAQSDAGAVKSKVAQLIVTASDETPCNPVPESYLIRLPHDCFQ NATNSFYDVGRCPV
KTCAGQQDNGIRCRDAVQNC CGISKTEEREIQCSGYTLPTKVAKECSCQRCTETR SIVRGRV
SAADNGEPMRFGHVYMGNSRVSM TGYKGTFTLHVPQDTERLVLT FVDRLQKFVNTTKVLPFN
KKGS AVFHEIKMLRRKEPIT LEAMETNIIPLGEVVGEDPMAELEIPSR SFYRQNGEPYIGKV
KASVTFLDPRNISTATAAQTDLNF INDEGDTFPLRTYGMFSVDFRDEVTSEPLNAGKVKVHL
DSTQVKMPEHISTVKLWSLNPDTGLWEEEGDFKFENQRRNKREDRTFLVGNLEIRERRLFNL
DVPESRRCFVKVRAYR SERFLPSEIQGVVISVINLEPRTGFLSNPRAWGRFDSVITGPNGA
CVPAFCDDQSPDAYSAYVLASLAGEELQAVESSPKFNPNAIGVPQPYLNKLN YRRTDHEDPR
VKKTAFQISMAKPRPN SAEESNGPIYAFENLRACEEAPPSAAHFRFYQIEGDRYDYNTVPFN
EDDPMSWTE DYLAWWPKPMEFRACYIKVKIVGPLEVNVR SRNMGGTHRRTVGKLYGIRDVRS
TRDRDQPNVSAACLEFKCSGMLYDQDRVDRTL VKVIPQGSRRASVNPMLHEYLVNHLPLAV
NNDTSEYTMLAPLDPLGHNYGIYTVTDQDPRTAKEIALGRCFDGTSDGSSRIMKSNVGVALT
FNCVERQVGRQSAFQYLQSTPAQSPAAGTVQGRVPSRRQQRASRGGRQGGVVASLRFPRVA
QQPLIN

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FIGURE 73

CTGCAAGTTGTTAACGCCTAACACACAAGTATGTTAGGCTTCCACCAAAGTCTCTCAATATAC
CTGAATACGCACAATATCTTAACTCTTCATATTTGGTTTTGGGATCTGCTTTGAGGTCCCAT
CTTCATTTAAAAAAAATACAGAGACCTACCTACCCGTACGCATACATACATATGTGTATAT
ATATGTAAACTAGACAAAGATCGCAGATCATAAAGCAAGCTCTGCTTTAGTTTCCAAGAAGA
TTACAAAGAATTTAGAGATGATTTTGTCAAGATCCCTGTGATTATGCCCCTTTGGGTTACG
GTGTCTCTCAGTGATGCAGCCCTACCCCTTGGTTTGGGGACATTATGATTTGTGTAAAGACTCA
GATTTACACGGAAGAAGGGAAAGTTTGGGATTACATGGCCTGCCAGCCGGAATCCACGGACA
TGACAAAATATCTGAAAGTGAACTCGATCCTCCGGATATTACCTGTGGAGACCCTCCTGAG
ACGTTCTGTGCAATGGGCAATCCCTACATGTGCAATAATGAGTGTGATGCGAGTACCCTGA
GCTGGCACACCCCCCTGAGCTGATGTTTGATTTTGAAGGAAGACATCCCTCCACATTTTGGC
AGTCTGCCACTTGGGAAGGAGTATCCCAAGCCTCTCCAGGTTAACATCACTCTGTCTTGGAGC
AAAACCATTTGAGCTAACAGACAACATAGTTTATTACCTTTGAATCTGGGCGTCCAGACCAAAT
GATCCTGGAGAAGTCTCTCGATTATGGACGAACATGGCAGCCCTATCAGTATTATGCCACAG
ACTGCTTAGATGCTTTTACATGGATCCTAAATCCGTGAAGGATTTATCACAGCATACGGTC
TTAGAAATCATTTGCAAGAAGAGTACTCAACAGGGTATACAACAAATAGCAAAATAATCCA
CTTTGAAATCAAAGACAGGTTTCGCGCTTTTGGCTGGACCTCGCCTACGCAATATGGCTTCCC
TCTACGGACAGCTGGATACAACCAAGAACTCAGAGATTTCTTTACAGTCACAGACCTGAGG
ATAAGGCTGTTAAGACCAGCCGTGGGGAAATATTTGTAGATGAGCTACACTTGGCAGCCTA
CTTTTACGCGATCTCAGACATAAAGGTGCGAGGAAGGTGCAAGTGAATCTCCATGCCACTG
TATGTGTGTATGACAACAGCAAATTTGACATGCGAATGTGAGCACAACACTACAGGTCCAGAC
TGTGGGAAATGCAAGAAGAATTATCAGGGCCGACCTTGGAGTCCAGGCTCCTATCTCCCAT
CCCCAAAGGCACGTGCAAATACCTGTATCCCCAGTATTTCCAGTATTTGGTACGAATGTCTGCG
ACAACGAGCTCCTGCACTGCCAGAACGGAGGGACGTGCCACAACAACGTGCGCTGCGCTGTGC
CCGGCCGCATACACGGGCATCCTCTGCGAGAAGCTGCGGTGCGAGGAGGCTGGCAGCTGCGG
CTCCGACTCTGGCCAGGGCGCGCCCCCGCACGGCACCCCAGCGCTGCTGCTGTGACCACGC
TGCTGGGAACCGCCAGCCCCCTGGTGTCTAGGTGTACCTCCAGCCACACCGGACGGGCCCT
GTGCCGTGGGGAAGCAGACACAACCCAAACATTTTGCTACTAACATAGGAAACACACATAC
AGACACCCCCACTCAGACAGTGTACAACTAAGAAGGCCTAACTGAACTAAGCCATATTTAT
CACCCGTGGACAGCACATCCGAGTCAAGACTGTTAATTTCTGACTCCAGAGGAGTTGGCAGC
TGTTGATATTATCACTGCAAATCACATTGCCAGCTGCAGAGCATATTGTGGATTGGAAAGGC
TGCGACAGCCCCCAAACAGGAAAGACAAAAACAAACAAATCAACCGACCTAAAAACATTG
GCTACTCTAGCGTGGTGGCCCTAGTACGACTCCGCCCAGTGTGTGGACCAACCAATAGCA
TTCTTTGCTGTGAGGTGCATTGTGGGCATAAGGAAATCTGTTACAAGCTGCCATATTGGCCT
GCTTCCGTCCCTGAATCCCTTCCAACCTGTGCTTTAGTGAACGTTGCTCTGTAAACCTCGTT
GGTTGAAAGATTTCTTTGTCTGATGTTAGTGATGCACATGTGTAACAGCCCCCTCTAAAAGC
GCAAGCCAGTCATACCCCTGTATATCTTAGCAGCACTGAGTCCAGTGCGAGCACACCCAC
TATACAAGAGTGGCTATAGGAAAAAAGAAAGTGATCTATCCTTTTGTATTCAAATGAAGTT
ATTTTCTTGAACTACTGTAATATGTAGATTTTTTGTATTATTGCCAATTTGTGTTACCAGA
CAATCTGTTAATGTATCTAATTCGAATCAGCAAAGACTGACATTTTATTTTGTCCCTCTTTG
TTCTGTTTTGTTTCACTGTGCAGAGATTTCTCTGTAAGGGCAACGAACGTGCTGGCATCAAA
GAATATCAGTTTACATATATAACAAGTGAATAAGATTCCACCAAAGGACATTCTAAATGTT
TTCTGTGTGCTTTAACACTGGAAGATTTAAAGAATAAAAACTCCTGCATAAACGATTTCAAG
AATTTGTATTGCAATTTCTTAAGATGAAAGGAACAGCCACCAAGCAGTTTCACACTCACTTT
ACTGATTTCTGTGTGGACTGAGTACATTCAGCTGACGAATTTAGTTCACAGGAAGATGGATT
GATGTTCACTAGCTTGGACAACCTCTGCAAAATATGAGACTATTTCCACTTGGGAAAAATTA
CAACAGCAAAAAAAAAAAAAAAAAAAAAA

FIGURE 74

MYLSRSLSIHALWVTVSSVMQPYPLVWGHYDLCKTQIYTEEGKVWDYMACQPESTDMTKYLK
VKLDPPDITCGDPPETFCAMGNPYMCNNECDASTPELAHPPELMFDFEGRHPSTFWQSATWK
EYPKPLQVNITLSWSKTIELTDNIVITFESGRPDQMILEKSLDYGRTWQPYQYYATDCLDAF
HMDPKSVKDLSQHTVLEI ICTEEYSTGYTTNSKIIHFEIKDRFALFAGPRLRNMASLYGQLD
TTKKLRDFFTVTDLRIRLLRPAVGEIFVDELHLARYFYAISDIKVRGRCKCNLHATVCVYDN
SKLTCECEHN'TTGPDCGKCKKNYQGRPWSPGSYLP I PKGTANTCIPSISSIGTNVCDNELLH
CQNGGTCHNNVRCLCPAAYTGILCEKLRCEEAGSCGSDSGQGAPPHGTPALLLLTTLLGTAS
PLVF

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FIGURE 75

CCCACGCGTCCGGGTGACCTGGGCCGAGCCCTCCCGGTCCGGCTAAGATTGCTGAGGAGGCGG
CGGGTAGCTGGCAGGCGCCGACTTCCGAAGGCCGCCGTCCGGGCGAGGTGTCCTCATGACTT
CTCTTGTGGACCATGTCCGTGATCTTTTTTGCCTGCGTGGTACGGGTAAGGGATGGACTGCC
CCTCTCAGCCTCTACTGATTTTTTACCACACCCAAGATTTTTTGGGAATGGAGGAGACGGCTCA
AGAGTTTAGCCTTGGCGACTGGCCCAGTATCCAGGTGAGGTCTGCAGAAGGTGTGACTTT
AGTATACATTTTTCTTCTTTTCGGGGACGTGGCCTGCATGGCTATCTGCTCCTGCCAGTGTCC
AGCAGCCATGGCCTTCTGCTTCCTGGAGACCTGTGGTGGGAATTCACAGCTTCCTATGACA
CTACCTGCATTGGCCTAGCCTCCAGGCCATACGCTTTTTCTTGAGTTTGACAGCATCATTAG
AAAGTGAAGTGGCATTTTAACTATGTAAGTTCCTCTCAGATGGAGTGCAGCTTGAAAAAAT
TCAGGAGGAGCTCAAGTTGCAGCCTCCAGCGGTTCTCACTCTGGAGGACACAGATGTGGCAA
ATGGGGTGATGAATGGTCACACACCGATGCACTTGGAGCCTGCTCCTAATTTCCGAATGGAA
CCAGTGACAGCCCTGGGTATCCTCTCCCTCATTCTCAACATCATGTGTGCTGCCCTGAATCT
CATTGAGGAGTTCACCTTGCAGAACATTCTTTACAGGATCCAAGGAGCTGGTTCTGCTGGT
TGGACCAAACCTCGTGAGCCAGCCACCCCTGACCCAAATGAGGAGAGCTCTGATTCTCCCAT
CCGGGAGCAGTGATGTCAAACCTTCTGCTGCTGGGGAAATCTCATCAGCAGGGAGCCTGTGGA
AAAGGGCATGTGAGTGAATCTGGGAATGGCTGGATTGCGAAACATCTGCCCATGTGTATTG
ATGGCAGAGCTGTTGCCCACAAGCGCCTTTTATTTAGGGTAAAATTAACAAATCCATTCTAT
TCCTCTGACCCATGCTTAGTACATATGACCTTTAACCCCTTACATTTATATGATTCTGGGGTT
GCTTCAGAAGTGTTATTTTCATGAATCATTCATATGATTTGATCCCCCAGGATTCTATTTTGT
TTAATGGGCTTTTCTACTAAAAGCATAAAATACTGAGGCTGATTTAGTCAGGGCAAAACCAT
TTACTTTACATATTCGTTTTCAATACTTGCTGTTTCATGTTACACAAGCTTCTTACGGTTTTTC
TTGTAACAATAAAATATTTTGAGTAAATAATGGGTACATTTTAACAAACTCAGTAGTACAACC
TAAACTTGTATAAAAGTGTGTAAAAATGTATAGCCATTTATATCCTATGTATAAATTAAATG
AGGTGGCTTCAGAAATGGCAGAATAAATCTAAAGTGTTTATTAAAAAATAAAAAAAAAAAAAA
AAAAG

FIGURE 76

MSVIFACVVRVRDGLPLSASTDFYHTQDFLEWRRRLKSLALRLAQYPGRGSAEGCDFSIHF
SSFGDVACMAICSCQCPAAMAFCFLETLWWEFTASYDTTCIGLASRPYAFLEFDSIIQVKW
HFNYVSSSQMECSLEKIQEELKLQPPAVLTLEDTDVANGVMNGHTPMHLEPAPNFRMEPVTA
LGILSLILNIMCAALNLIRGVHLAEHSLQDPRSWFCWLDQTS

FIGURE 77

TGCTTCCTGGAGACCCTGTGGTGGGAATTCACAGCTTCNTATGACACTACCTGCATTGGCNT
AGCCTCCAGGCCATACGCCTTTCTTGAGTTTGACAGCATCATTGAGAAAGTGAAGTGGCATT
TTAACTATGTAAGTTCCTNTCAGATGGAGTGCAGCTTGGAAAAAATTCAGGAGGAGCTCAAG
TTGCAGCCTCCAGCGGTTCTCANTATGGAGGACACAGATGTGGCAAATGGGGT

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FIGURE 78

CTCAGCGGCGCTTCCTCGTAGCGAGCCTAGTGGCGGGTGTTTGCATTGAAACGTGAGCGCGA
CCCGACCTTAAAGAGTGGGGAGCAAAGGGAGGACAGAGCCCTTTAAACGAGGCGGGTGGTG
CCTGCCCCCTTTAAGGGCGGGGCGTCCGGACGACTGTATCTGAGCCCCAGACTGCCCCGAGTT
TCTGTGCGCAGGCTGCGAGGAAAGGCCCTAGGCTGGGTCTGGGTGCTTGGCGGCGGCGGCTT
CCTCCCCGCTCGTCCTCCCCGGGCCCAGAGGCACCTCGGCTTCAGTCATGCTGAGCAGAGTA
TGGAAGCACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGC
GAGTGTATTATATCAACACTTCTGTTTGAACACTGTACATCCTCTGCCACATCTTCTTGAC
CCGCTTCAAGAAGCCTGCTGAGTTCACCACAGTGGATGATGAAGATGCCACCGTCAACAAGA
TTGCGCTCGAGCTGTGCACCTTTACCCTGGCAATTGCCCTGGGTGCTGTCTGCTCCTGCC
TTCTCCATCATCAGCAATGAGGTGCTGCTCTCCCTGCCTCGGAACACTACTACATCCAGTGGCT
CAACGGCTCCCTCATCCATGGCCTCTGGAACCTTGTTTTCTCTTCCCCAACCTGTCCCTCA
TCTTCTCATGCCCTTTGCATATTTCTTCACTGAGTCTGAGGGCTTTGCTGGCTCCAGAAAG
GGTGTCTTGGGCGGGTCTATGAGACAGTGGTGATGTTGATGCTCCTCACTCTGCTGGTGCT
AGGTATGGTGTGGGTGGCATCAGCCATTGTGGACAAGAACAAGGCCAACAGAGAGTCACTCT
ATGACTTTTGGGAGTACTATCTCCCTACCTCTACTCATGCATCTCCTTCCTTGGGGTTCTG
CTGCTCCTGGTGTGTACTCCACTGGGTCTCGCCCGCATGTTCTCCGTCACTGGGAAGCTGCT
AGTCAAGCCCCGGCTGCTGGAAGACCTGGAGGAGCAGCTGTACTGCTCAGCCTTTGAGGAGG
CAGCCCTGACCCGAGGATCTGTAATCCTACTTCTGCTGGCTGCCTTTAGACATGGAGCTG
CTACACAGACAGGTCTGGCTCTGCAGACACAGAGGGTCTGCTGGAGAAGAGGCGGAAGGC
TTCAGCCTGGCAACGGAACCTGGGCTACCCCTGGCTATGCTGTGCTTGTGCTGCTGACGG
GCCTGTCTGTGCTCATTGTGGCCATCCACATCCTGGAGCTGCTCATCGATGAGGCTGCCATG
CCCCGAGGCATGCAGGGTACCTCCTTAGGCCAGGTCTCCTTCTCCAAGCTGGGCTCCTTTGG
TGCCGTCAATTCAGGTGTACTCATCTTTTACCTAATGGTGTCTCAGTTGTGGGCTTCTATA
GCTCTCCACTCTTCCGGAGCCTGCGGCCCAGATGGCACGACACTGCCATGACGCAGATAATT
GGGAAGTGTGTCTGTCTCCTGGTCCTAAGCTCAGCACTTCCTGTCTTCTCTCGAACCCTGGG
GCTCACTCGCTTTGACCTGCTGGGTGACTTTGGACGCTTCAACTGGCTGGGCAATTTCTACA
TTGTGTTCTCTACAACGCAGCCTTTGCAGGCCTCACCACACTCTGTCTGGTGAAGACCTTC
ACTGCAGCTGTGCGGGCAGAGCTGATCCGGGCCTTTGGGCTGGACAGACTGCCGCTGCCCGT
CTCCGGTTTCCCCCAGGCATCTAGGAAGACCCAGCACCAGTGAACCTCCAGCTGGGGGTGGGA
AGGAAAAAACTGGACACTGCCATCTGCTGCCTAGGCCTGGAGGGAAGCCCAAGGCTACTTGG
ACCTCAGGACCTGGAATCTGAGAGGGTGGGTGGCAGAGGGGAGCAGAGCCATCTGCACTATT
GCATAATCTGAGCCAGAGTTTGGGACCAGGACCTCCTGCTTTTCCATACTTAACTGTGGCCT
CAGCATGGGGTAGGGCTGGGTGACTGGGTCTAGCCCCCTGATCCCAAATCTGTTTACACATCA
ATCTGCCTCACTGCTGTTCTGGGCCATCCCCATAGCCATGTTTACATGATTTGATGTGCAAT
AGGGTGGGGTAGGGGAGGAAAGGACTGGGCCAGGGCAGGCTCGGGAGATAGATTGTCTCC
CTTGCTCTGGCCCAGCAGAGCCTAAGCACTGTGCTATCCTGGAGGGGCTTTGGACCACCTG
AAAGACCAAGGGGATAGGGAGGAGGAGGCTTCAGCCATCAGCAATAAAGTTGATCCCAGGGA
AAAAAA

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FIGURE 79

MEAPDYEVLSVREQLFHERIRECTISTLLFATLYILCHIFLTRFKKPAEFTTVDDDEDATVVK
IALELCTFTLAIALGAVLLLPPFSIISNEVLLSLPRNYITQWLNGSLIHGLWNLVFLFPNLSL
IFLMPFAYFFTESEGFAGSRKGVLRVYETVVMLMLLTLLVLGMVWVASAIVDKNKANRESL
YDFWEYYLPYLYSCISFLGVLLLLVCTPLGLARMFSVTGKLLVKPRLLEDLEEQLYCSAFEE
AALTRRICNPTSCWLPDMELLHRQVLALQTQRVLLEKRRKASAWQRNLGYPLAMLCLLVLT
GLSVLIVAIHILELLIDEAAMPGRMQGTSLGQVSFSKLGSGGAVIQVVLIFYLMVSSVVGFY
SSPLFRSLRPRWHDAMTQIIGNCVCLLVLSALPVFSRTLGLTRFDLLGDFGRFNWLGIFY
IVFLYNAAFAGLTTLCLVKTFTA AVRAELIRAFGLDRLPLPVSGFPQASRKTQHQ

FIGURE 80

GGCTGCCGAGGGAAGGCCCTTGGGTTGGTCTTGGTTGCTTGGCGGCGGCGGNTTCNTCCCC
~~GCTCGTCCTCCCCGGGCCCCAGAGGCCACCTCGGCTTCAGTCATGCTGAGCAGAGTATGGAAGC~~
ACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGCGAGTGTA
TTATATCAACACTTCTGTTTGCAACACTGTACATCCTCTGCCACATCTTCCTGACCCGCTTC
AAGAAGCCTGCTGAGTTCACCACAGTGGATGATGAAGATGCCACCG

FIGURE 81

GACCGACCTTAAAGAGTGGGAGCAAAGGGAGGACAGAGCCTTTTAAAACGAGGCGGTGGTG
CTGCCCTTTAAGGGCGGGCGTCCGGACGACTGTATCTGAGCCCCAGACTGCCCCGAGTTTC
TGTCGCAGGCTGCGAGGAAAGGCCCCCTAGGCTGGGTCTGGTGCTTGGCGGCGGCGGCTTCCT
CCCCGTTGTCNTCCCCGGGCCAGAGGCACCTCGGCTTCAGTCATGCTGAGCAGAGTATGGA
AGCACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGCGAGT
GTATTATATCAACACTTCTGTTTGCAACACTGTACATCNTCTGCCACATCTTCCTGACCCGC
TTCAAGAAGCCTGCTGAGTTCACCACAGTGGATGATGAAGATGCCACCGTCAACAAGATTGC
GCTCGAGCTGTGCACCTTTACCCTGGCAATTGCCCTGGGTGCTGTCCTGCTCCTGCCCTTCT
CCATCATCAGCAATGAGGTGCTGCACTCCC

FIGURE 82

GATGTGCTCCTTGGAGCTGGTGTGCAGTGTCTGACTGTAAGATCAAGTCCAAACCTGTTTT
GGAATTGAGGAACTTCTCTTTTGATCTCAGCCCTTGGTGGTCCAGGTCTTCATGCTGCTGT
GGGTGATATTACTGGTCCTGGCTCCTGTCAGTGGACAGTTTGCAAGGACACCCAGGCCCAT
ATTTTCCTCCAGCCTCCATGGACCACAGTCTTCCAAGGAGAGAGAGTGACCCTCACTTGCAA
GGGATTTGCTTCTACTCACCACAGAAAACAAAATGGTACCATCGGTACCTTGGGAAAGAAA
TACTAAGAGAAAACCCAGACAATATCCTTGAGGTTTCAGGAATCTGGAGAGTACAGATGCCAG
GCCCAGGGCTCCCCCTCTCAGTAGCCCTGTGCACTTGGATTTTTCTTCAGAGATGGGATTTCC
TCATGCTGCCCAGGCTAATGTTGAACTCCTGGGCTCAAGTGATCTGCTCACCTAGGCCTCTC
AAAGCGCTGGGATTACAGCTTCGCTGATCCTGCAAGCTCCACTTTCTGTGTTTGAAGGAGAC
TCTGTGGTTCTGAGGTGCCGGGCAAAGGCGGAAGTAACACTGAATAATACTATTTACAAGAA
TGATAATGTCCTGGCATTCTTAATAAAAGAACTGACTTCCAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 83

MLLWVILLVLAPVSGQFARTPRP11FLQPPWTTVFQGERVILTCKGFRFYSPQKTKWYHRYL
GKEILRETPDNILEVQESGEYRCQAQGSPLSSPVHLD FSSEMGFPHAAQANVELLGSSDLLT

FIGURE 84

CAGAAGAGGGGGCTAGCTAGCTGTCTCTGCGGACCAGGGAGACCCCGCGCCCCCGGTGT
GAGGCGGCCTCACAGGGCCGGGTGGGCTGGCGAGCCGACGCGGCGGCGGAGGAGGCTGTGAG
GAGTGTGTGGAACAGGACCCGGGACAGAGGAACCATGGCTCCGCAGAACCTGAGCACCTTTT
GCCTGTTGCTGCTATACCTCATCGGGGCGGTGATTGCCGGACGAGATTTCTATAAGATCTTG
GGGGTGCCTCGAAGTGCCCTCTATAAAGGATATTAAAAAGGCCTATAGGAACTAGCCCTGCA
GCTTCATCCCGACCGGAACCTGATGATCCACAAGCCAGGAGAAATTCAGGATCTGGGTG
CTGCTTATGAGGTTCTGTCAGATAGTGAGAAACGGAAACAGTACGATACTTATGGTGAAGAA
GGATTAAAGATGGTCATCAGAGCTCCCATGGAGACATTTTTTTCACACTTCTTTGGGGATTT
TGGTTTCATGTTTGGAGGAACCCCTCGTCAGCAAGACAGAAATATTCCAAGAGGAAGTGATA
TTATTGTAGATCTAGAAGTCACTTTGGAAGAAGTATATGCAGGAAATTTTGTGGAAGTAGTT
AGAAACAAACCTGTGGCAAGGCAGGCTCCTGGCAAACGGAAGTGCAATTGTGCGCAAGAGAT
GCGGACCACCCAGCTGGGCCCTGGGCGCTTCCAAATGACCCAGGAGGTGGTCTGCGACGAAT
GCCCTAATGTCAAACCTAGTGAATGAAGAACGAACGCTGGAAGTAGAAATAGAGCCTGGGGTG
AGAGACGGCATGGAGTACCCCTTTATTGGAGAAGGTGAGCCTCACGTGGATGGGGAGCCTGG
AGATTTACGGTTCCGAATCAAAGTTGTCAAGCACCCAATATTTGAAAGGAGAGGAGATGATT
TGTACACAAATGTGACAATCTCATTAGTTGAGTCACTGGTTGGCTTTGAGATGGATATTACT
CACTTGGATGGTCACAAGGTACATATTTCCCGGGATAAGATCACCAGGCCAGGAGCGAAGCT
ATGGAAGAAAGGGGAAGGGCTCCCCAACTTTGACAACAACAATATCAAGGGCTCTTTGATAA
TCACTTTTGATGTGGATTTTCCAAAAGAACAGTTAACAGAGGAAGCGAGAGAAGGTATCAAA
CAGCTACTGAAACAAGGGTCAGTGCAGAAGGTATACAATGGACTGCAAGGATATTGAGAGTG
AATAAAATTGGACTTTGTTTAAAATAAGTGAATAAGCGATATTTATTATCTGCAAGGTTTTT
TTGTGTGTGTTTTTGTTTTTATTTTCAATATGCAAGTTAGGCTTAATTTTTTTTATCTAATGA
TCATCATGAAATGAATAAGAGGGCTTAAGAATTTGTCCATTTGCATTTCGAAAAGAATGACC
AGCAAAAGGTTTACTAATACCTCTCCCTTTGGGGATTTAATGTCTGGTGCTGCCGCCCTGAGT
TTCAAGAATTAAAGCTGCAAGAGGACTCCAGGAGCAAAGAAACACAATATAGAGGGTTGGA
GTTGTTAGCAATTTCAATTCAAAATGCCAACTGGAGAAGTCTGTTTTTAAATACATTTTGTG
TTATTTTTTA

FIGURE 85

MAPQNLSTFCLLLLYLIGAVIAGRDFYKILGVPRASIKDIKKAYRKLALQLHPDRNPDPPQ
AQEKFDLGAAYEVLSDSEKQYDQTYGEEGLKDGHQSSHGDI FSHFFGDFGFMFGGTTPRQQ
DRNIPRGSDIIVDLEVTLEEVYAGNFVEVVRNKPVARQAPGKRKCNCRQEMRTTQLGPGRFQ
MTQEVVCDPCPNVCLVNEERTLEVEIEPGVRDGMETPFGEPEPHVDGEPGDLRFRIKVVKH
PIFERRGDDLYTNVTISLVESLVGFEMDITHLDGHKVHISRDKITRPGAKLWKKGEGLPNFD
NNNIKGSIIITFDVDFPKEQLTEEAREGIKQLLKQGSVQKVYNGLQGY

FIGURE 86

TGGGACCAGGGAACCCCGGGCCCCCGGTGGAGNGCCTAACAGGCCGGTGGNTGCGACCGAA
GCGGCCGGGCGGAGGAGGTTTTGAGGATTTTTGGAACAGGACCCGGACAGAGGAACCATGGTT
CCGCAGAACNTGAGCACNTTTTGCCTGTTGNTGNTATACTTCATCGGGGCGGTGATTGCCGG
ACGAGATTTNTATAAGATTTTGGGGTGCCTNGAAGTGCCTTNTATAAAGGATATTAAAAAGG
CCTATAGGAACTAGCCCTGCAGNTTATCCCGACCGGAACCCCTGATGATCCACAAGCCCAG
GAGAAATTCAGGATTTGGGTGCTGCTTATGAGGTTNTGTCAGATAGTGAGAAACGGAAACA
GTACGATAATTATGGTGAAGAAGGATTAAAAGATGGTNATCAGAGCTCCCATGGAGACATTT
TTTCACACTTNTTTGGGGATTTTGGTTTCATGTTTGGAGGAACCCCTNGTCAGCAAGACAGA
AATATTCCAAGAG

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FIGURE 87

GGCACGAGGCGGCGGGGCAGTCGCGGGATGCGCCCGGGAGCCACAGCCTGAGGCCCTCAGGT
CTCTGCAGGTGTCGTGGAGGAACCTAGCACCTGCCATCCTCTTCCCCAATTTGCCACTTCCA
GCAGCTTTAGCCCATGAGGAGGATGTGACCGGGACTGAGTCAGGAGCCCTCTGGAAGCATGG
AGACTGTGGTGATTGTTGCCATAGGTGTGCTGGCCACCATCTTTCTGGCTTCGTTTGAGCC
TTGGTGCTGGTTTGCAGGCAGCGCTACTGCCGCGCGAGACCTGCTGCAGCGCTATGATTC
TAAGCCCATTGTGGACCTCATTGGTGCCATGGAGACCCAGTCTGAGCCCTCTGAGTTAGAAC
TGGACGATGTCGTTATCACCAACCCCCACATTGAGGCCATTCTGGAGAATGAAGACTGGATC
GAAGATGCCTCGGGTCTCATGTCCCACTGCATTGCCATCTTGAAGATTTGTCACTCTGAC
AGAGAAGCTTGTGGCATGACAATGGGCTCTGGGGCCAAGATGAAGACTTCAGCCAGTGTCA
GCGACATCATTGTGGTGGCCAAGCGGATCAGCCCCAGGGTGGATGATGTTGTGAAGTCGATG
TACCCTCCGTTGGACCCCAAACCTCCTGGACGCACGGACGACTGCCCTGCTCCTGTCTGTCA
TCACCTGGTGCTGGTGACAAGGAATGCCTGCCATCTGACGGGAGGCCTGGACTGGATTGACC
AGTCTCTGTGCGGCTGCTGAGGAGCATTTGGAAGTCCTTCGAGAAGCAGCCCTAGCTTCTGAG
CCAGATAAAGGCCTCCAGGCCCTGAAGGCTTCCTGCAGGAGCAGTCTGCAATTTTAGGCCT
ACAGGCCAGCAGCTAGCCATGAAGGCCCCCTGCCGCCATCCCTGGATGGCTCAGCTTAGCCTT
CTACTTTTTCTATAGAGTTAGTTGTTCTCCACGGCTGGAGAGTTCAGCTGTGTGTGCATAG
TAAAGCAGGAGATCCCCGTCAGTTTATGCCTCTTTTGCAGTTGCAAACTGTGGCTGGTGAGT
GGCAGTCTAATACTACAGTTAGGGGAGATGCCATTCACTCTCTGCAAGAGGAGTATTGAAAA
CTGGTGGACTGTGAGCTTTATTTAGCTCACCTAGTGTCTTCAAGAAAATTGAGCCACCGTCT
AAGAAATCAAGAGGTTTACATTAAAATTAGAATTTCTGGCCTCTCTCGATCGGTGAGAATG
TGTGGCAATTCTGATCTGCATTTTCAGAAGAGGACAATCAATTGAACTAAGTAGGGGTTTC
TTCTTTTGGCAAGACTTGTACTCTCTCACCTGGCCTGTTTCATTTATTTGTATTATCTGCCT
GGTCCCTGAGGCGTCTGGGTCTCTCCTCTCCCTTGCAAGTTTGGGTTTGAAGCTGAGGAACT
ACAAAGTTGATGATTTCTTTTTTATCTTTATGCCTGCAATTTTACCTAGCTACCACTAGGTG
GATAGTAAATTTATACTTATGTTTCCCTCAAAAAAAAAAAAAA

FIGURE 88

METVVIVAIGVLATIFLASFAALVLVCRQRYCRPRDLLQRYDSKPIVDLIGAMETQSEPSEL

~~ELDDVVTMTNPHTAILENEDWTEDASGLMSHGTATLKTCHTLTEKLVAMTMGSCAKMKTSA~~

VSDIIVVAKRISPRVDDVVKSMYPPLDPKLLDARTTALLSVSHLVLVTRNACHLTGGLDWI

DQSLSAEEHLEVLREAALASEPDKGLPGPEGFLQEQSAI

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FIGURE 89

GCTTCATTTCTCCCGACTCAGCTTCCCACCCTGGGCTTCCGAGGTGCTTTCGCCGCTGTCC
CCACCACTGCAGCCATGATCTCCTTAACGGACACGCAGAAAATTGGAATGGGATTAACAGGA
TTTGGAGTGTTTTCTGTCTTTGGAATGATTCTCTTTTTTGACAAAGCACTACTGGCTAT
TGGAAATGTTTTATTTGTAGCCGGCTTGGCTTTTGTAATTGGTTTAGAAAGAACATTCAGAT
TCTTCTTCCAAAAACATAAAATGAAAGCTACAGGTTTTTTTTCTGGGTGGTGTATTTGTAGTC
CTTATTGGTTGGCCTTTGATAGGCATGATCTTCGAAATTTATGGATTTTTCTCTTGTT CAG
GGGCTTCTTCCGTGTCGTTGTTGGCTTTATTAGAAGAGTGCCAGTCCTTGGATCCCTCCTAAAT
TTACCTGGAATTAGATCATTTGTAGATAAAGTTGGAGAAAGCAACAATATGGTATTAACAACA
AGTGAATTTGAAGACTCATTTAAAATATTGTGTTATTTATAAAGTCATTTGAAGAATATTCA
GCACAAAATTAAATTACATGAAATAGCTTGTAATGTTCTTTACAGGAGTTTAAAACGTATAG
CCTACAAAGTACCAGCAGCAAATTAGCAAAGAAGCAGTGAAAACAGGCTTCTACTCAAGTGA
ACTAAGAAGAAGTCAGCAAGCAAAGCTGAGAGAGGTGAAATCCATGTTAATGATGCTTAAGAA
ACTCTTGAAGGCTATTTGTGTTGTTTTCCACAATGTGCGAAACTCAGCCATCCTTAGAGAA
CTGTGGTGCCTGTTTCTTTCTTTTTATTTTGAAGGCTCAGGAGCATCCATAGGCATTTGCT
TTTTAGAAGTGTCCTGCAATGGCAAAAATATTTCCAGTTGCACTGTATCTCTGGAAGTGA
TGCATGAATTCGATTGGATTGTGTCATTTTAAAGTATTAAAACCAAGGAAACCCCAATTTTG
ATGTATGGATTACTTTTTTTTTGNGCNCAGGGCC

FIGURE 90

MISLTDQTQKIGMGLTGFGVFFLFFGMILFFDKALLAIGNVLFVAGLAFVIGLERTFRFFFQK
HKMKATGFFLGGVFVVLIGWPLIGMIFEIYGFFLLFRGFFPVVVGFIIRVPVLGSLLNLPGI
RSFVDKVGESNNMV

Important features:

Transmembrane domains:

amino acids 12-30 (typeII), 33-52, 69-89 and 93-109

N-myristoylation sites.

amino acids 11-16, 51-56 and 116-121

Aminoacyl-transfer RNA synthetases class-II protein.

amino acids 49-59

FIGURE 91

GAAGACGTGGCGGCTCTCGCCTGGGCTGTTTCCCGGCTTCATTTCTCCCGACTCAGCTTCCC
ACCNTGGGCTTTCCGAGGTGCTTTCGCCGCTGTCCCCA[~]CCACTGCAGCCATGATCTCCTTAA
CGGACACGCAGAAAAATTGGAATGGGATTAACCGGATTTGGAGTGTTTTTCCTGTTCTTTGGA
ATGATTCTCTTTTTTGACAAAGCACTACTGGCTATTGGAAATGTTTTATTTGTAGCCGGCTT
GGCTTTTGTAATTGGTTTAGAAAGAACATTCAGATTCTTCTTCCAAAAACATAAAATGAAAG
CTACAGGTTTTTTTTCTGGGTGGTGTATTTGTAGTCCTTATTGGTTGGCCTTTGATAGGCATG
ATCTTCGAAATTTATGGATTTTTTCTCTTGTTT

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FIGURE 92

GGCACGAGGCTGAACCCAGCCGGCTCCATCTCAGCTTCTGGTTTCTAAGTCCATGTGCCAAA
GGCTGCCAGGAAGGAGACGCCTTCCTGAGTCCTGGATCTTTCTTCCTTCTGGAAATCTTTGA
CTGTGGGTAGTTATTTATTTCTGAATAAGAGCGTCCACGCATCATGGACCTCGCGGGACTGC
TGAAGTCTCAGTTCCTGTGCCACCTGGTCTTCTGCTACGTCTTTATTGCCTCAGGGCTAATC
ATCAACACCATTTCAGCTCTTCACTCTCCTCCTCTGGCCCATTAACAAGCAGCTCTTCCGGAA
GATCAACTGCAGACTGTCCTATTGCATCTCAAGCCAGCTGGTGATGCTGCTGGAGTGGTGGT
CGGGCACGGAATGCACCATCTTCACGGACCCGCGCGCTACCTCAAGTATGGGAAGGAAAAT
GCCATCGTGGTTCTCAACCACAAGTTTGAAATTGACTTTCTGTGTGGCTGGAGCCTGTCCGA
ACGCTTTGGGCTGTTAGGGGGCTCCAAGGTCTGGCCAAGAAAGAGCTGGCCTATGTCCCAA
TTATCGGCTGGATGTGGTACTTCACCGAGATGGTCTTCTGTTCGCGCAAGTGGGAGCAGGAT
CGCAAGACGGTTGCCACCAGTTTGCAGCACCTCCGGGACTACCCCGAGAAGTATTTTTTCT
GATTCACTGTGAGGGCACACGGTTCACGGAGAAGAAGCATGAGATCAGCATGCAGGTGGCCC
GGGCAAGGGGCTGCCTCGCCTCAAGCATCACCTGTTGCCACGAACCAAGGGCTTCGCCATC
ACCGTGAGGAGCTTGAGAAATGTAGTTTTCAGCTGTATATGACTGTACACTCAATTTCAGAAA
TAATGAAAATCCAACACTGCTGGGAGTCCTAAACGGAAAGAAATACCATGCAGATTTGTATG
TTAGGAGGATCCCACTGGAAGACATCCCTGAAGACGATGACGAGTGCTCGGCCTGGCTGCAC
AAGCTCTACCAGGAGAAGGATGCCTTTTCAGGAGGAGTACTACAGGACGGGCACCTTCCCAGA
GACGCCCATGGTGCCCCCGGCGGCCCTGGACCCTCGTGAAGTGGCTGTTTTGGGCCTCGC
TGGTGCTCTACCCTTTCTTCCAGTTCCTGGTCAGCATGATCAGGAGCGGGTCTTCCCTGACG
CTGGCCAGCTTCATCCTCGTCTTCTTTGTGGCCTCCGTGGGAGTTCGATGGATGATTGGTGT
GACGGAAATTGACAAGGGCTCTGCCTACGGCAACTCTGACAGCAAGCAGAACTGAATGACT
GACTCAGGGAGGTGTCACCATCCGAAGGGAACCTTGGGGAACTGGTGGCCTCTGCATATCCT
CCTTAGTGGGACACGGTGACAAAGGCTGGGTGAGCCCCCTGCTGGGCACGGCGGAAGTCACGA
CCTCTCCAGCCAGGAGTCTGGTCTCAAGGCCGATGGGGAGGAAGATGTTTTGTAATCTTT
TTTTCCCCATGTGCTTTAGTGGGCTTTGGTTTTCTTTTTGTGCGAGTGTGTGTGAGAATGGC
TGTGTGGTGAGTGTGAACTTTGTCTGTGATCATAGAAAGGTATTTTAGGCTGCAGGGGAG
GGCAGGGCTGGGGACCGAAGGGGACAAGTTCCCTTTTCATCCTTTGGTGCTGAGTTTCTGT
AACCTTGGTTGCCAGAGATAAAGTGAAAAGTGCTTTAGGTGAGATGACTAAATTATGCCTC
CAAGAAAAAAAAAATTAAAGTGCTTTTCTGGGTCAAAAAAAAAA

FIGURE 93

MDLAGLLKSQFLCHLVFCYVFIA SGLIINTIQLF TLLLWPINKQLFRKINCRLSYCISSQLV
MLEWWSGTECTIFTDPRAYLKYGKENAIVVLN HKFEIDFLCGWSLSERFGLLGGSKVLAKK
ELAYVPIIGWMWYFTEMVFCSRKEQDRKTVATSLQH LRDYPEKYFFLIHCEGTRFTEKKHE
ISMQVARAKGLPRLKHLLPRTKGFAITVRS LRNVVSAVYDCTLNFRNNENPTLLGV LNKKK
YHADLYVRRIPLEDIPEDDDECSAWLHKLYQE KDAFQEEYYRTGTFPETPMVPPRRPWT LVN
WLFWASLVLYPFFQFLVSMIRSGSSLTLASFILV FFFVASVGVRWMIGVTEIDKGSAYGNSDS
KQKLND

FIGURE 94

CTGAGGCGGCGGTAGCATGAGGGGGAGAGTACGTCGGCGGTGCTCTCGGGCTTTGTGCTCG
GCGCACTCGCTTTCCAGCACCTCAACACGGACTCGGACACGGAAGGTTTTCTTCTTGGGGAA
GTAAAAGGTGAAGCCAAGAACAGCATTACTGATTCCCAAATGGATGATGTTGAAGTTGTTTA
TACAATTGACATTAGAAATATATTCCATGCTATCAGCTTTTGTAGCTTTTATAATTCTTCAG
GCGAAGTAAATGAGCAAGCACTGAAGAAAATATTATCAAATGTCAAAAAGAATGTGGTAGGT
TGGTACAAATTCGTCGTCAATTCAGATCAGATCATGACGTTTAGAGAGAGGCTGCTTCACAA
AACTTGCAGGAGCATTTTTCAAACCAAGACCTTGTTTTCTGCTATTAACACCAAGTATAA
TAACAGAAAAGCTGCTCTACTCATCGACTGGAACATTCCTTATATAAACCTCAAAAAGGACTT
TTTCACAGGGTACCTTTAGTGGTTGCCAATCTGGGCATGTCTGAACAACTGGGTATATAAAC
TGTATCAGGTTCCCTGTATGTCCACTGGTTTTAGCCGAGCAGTACAAACACACAGCTCTAAAT
TTTTTGAAGAAGATGGATCCTTAAAGGAGGTACATAAGATAAATGAAATGTATGCTTCATTA
CAAGAGGAATTAAAGAGTATATGCAAAAAAGTGGAAGACAGTGAACAAGCAGTAGATAAACT
AGTAAAGGATGTAAACAGATTAAACGAGAAATTGAGAAAAGGAGAGGAGCACAGATTCAGG
CAGCAAGAGAGAAGAACATCCAAAAAGACCTCAGGAGAACATTTTTCTTTGTGTCAGGCATTA
CGGACCTTTTTTCCAAATTCTGAATTTCTTCATTATGTGTTATGTCTTTAAAAAATAGACA
TGTTTCTAAAAGTAGCTGTAACCTACAACCACCATCTCGATGTAGTAGACAATCTGACCTTAA
TGGTAGAACACACTGACATTCCTGAAGCTAGTCCAGCTAGTACACCACAAATCATTAAGCAT
AAAGCCTTAGACTTAGATGACAGATGGCAATTCAAGAGATCTCGGTTGTTAGATACACAAGA
CAAACGATCTAAAGCAAATACTGGTAGTAGTAACCAAGATAAAGCATCCAAAAATGAGCAGCC
CAGAAACAGATGAAGAAATTGAAAAGATGAAGGGTTTTGGTGAATATTCACGGTCTCCTACA
TTTTGATCCTTTTAACCTTACAAGGAGATTTTTTTATTTGGCTGATGGGTAAAGCCAAACAT
TTCTATTGTTTTTACTATGTTGAGCTACTTGCAGTAAGTTCATTTGTTTTTACTATGTTTAC
CTGTTTGCAGTAATACACAGATAACTCTTAGTGCATTTACTTCACAAAGTACTTTTTTCAAAC
ATCAGATGCTTTTATTTCCAAACCTTTTTTTCACCTTTCACTAAGTTGTTGAGGGGAAGGCT
TACACAGACACATTCCTTAGAATTGGAAAAAGTGAGACCAGGCACAGTGGCTCACACCTGTAA
TCCCAGCACTTAGGGAAGACAAGTCAGGAGGATTGATTGAAGCTAGGAGTTAGAGACCAGCC
TGGGCAACGTATTGAGACCATGTCTATTAATAAATAAATGAAAAAGCAAGAATAGCCTTAT
TTTCAAAATATGGAAGAAATTTATATGAAAAATTTATCTGAGTCATTAAAATTCTCCTTAAG
TGATACTTTTTTAGAAGTACATTATGGCTAGAGTTGCCAGATAAAATGCTGGATATCATGCA
ATAAATTTGCAAAACATCATCTAAAAATTTAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 95

MEGESTSAVLSGFVLGALAFQHLNTSDTEGFLLEVKGEAKNSITDSQMDDVEVVYTTIDIQ
KYIPCYQLFSFYNSSGEVNEQALKKILSNVKKNVVGWYKFRRHSDQIMTFRERLLHKNLQEH
FSNQDLVFLLLTPSIITESCSTHRLEHSLYKPQKGLFHRVPLVVANLGMSEQLGYKTVSGSC
MSTGFSRAVQTHSSKFFEEEDGSLKEVHKINEMYASLQEELKSI CKKVEDSEQAVDKLVKDVN
RLKREIEKRRGAQIQAAAREKNIQKDPQENIFLCQALRTFFPNSEFLHSCVMSLKNRHVSKSS
CNYNHLDVVDNLTLMVEHTDIPEASPASTPQIIKHKALDLDLDRWQFKRSRLDQDKRSKA
NTGSSNQDKASKMSSPETDEEIEKMKGFGEYSRSPTE

FIGURE 96

GGCACAGCCGCGCGGCGGAGGGCAGAGTCAGCCGAGCCGAGTCCAGCCGGACGAGCGGACCA
GCGCAGGGCAGCCCAAGCAGCGCGCAGCGAACGCCCGCCGCGCCACACCCCTCTGCGGTCC
CCGCGGCGCCTGCCACCCCTTCCCTCCTTCCCCGCGTCCCCGCTCGCCGGCCAGTCAGCTTG
CCGGGTTGCTGCCCCGCGAAACCCGAGGTACCAGCCCGCGCCTCTGCTTCCCTGGGCCG
CGCGCCGCTCCACGCCCTCCTTCTCCCCGCGTCTCCTCCGCTGCTCGCCTCTTCCACCA
GACGCGAGGCCAGCTCTACTTTTCCCCCGCGTCTCCTCCGCTGCTCGCCTCTTCCACCA
ACTCCAACCTCCTTCTCCCTCCAGCTCCACTCGCTAGTCCCCGACTCCGCCAGCCCTCGGCC
GCTGCCGTAGCGCCGCTTCCCGTCCGGTCCCAAAGGTGGGAACGCGTCCGCCCCGGCCCCGA
CCATGCGACGGTTGCGCTTCCCCGCGCTTCTCTGCACCCCTGGCAGTGCTCAGCGCCGCGCTG
CTGGCTGCCGAGCTCAAGTCGAAAAGTTGCTCGGAAGTGCGACGCTTTTACGTGTCCAAAGG
CTTCAACAAGAACGATGCCCCCTCCACGAGATCAACGGTGATCATTGGAAGATCTGTCCCC
AGGGTTCTACCTGCTGCTCTCAAGAGATGGAGGAGAAGTACAGCCTGCAAAGTAAAGATGAT
TTCAAAGTGTTGGTCAGCGAACAGTGCAATCATTTGCAAGCTGTCTTTGCTTACGTTACAA
GAAGTTTGATGAATTTCTTCAAAGAACTACTTGAAAATGCAGAGAAATCCCTGAATGATATGT
TTGTGAAGACATATGGCCATTTATACATGCAAAATTTCTGAGCTATTTAAAGATCTCTTCGTA
GAGTTGAAACGTTACTACGTGGTGGGAAATGTGAACCTGGAAGAAATGCTAAATGACTTCTG
GGCTCGCCTCCTGGAGCGGATGTTCCGCTGGTGAACTCCAGTACCACTTTACAGATGAGT
ATCTGGAATGTGTGAGCAAGTATACGGAGCAGCTGAAGCCCTTCGGAGATGTCCCTCGCAA
TTGAAGCTCCAGGTTACTCGTGCTTTTGTAGCAGCCCGTACTTTTCGTCAAGGCTTAGCGGT
TGCGGGAGATGTGCTGAGCAAGGTCTCCGTGGTAAACCCACAGCCAGTGTAACCATGCCC
TGTTGAAGATGATCTACTGCTCCCACTGCCGGGGTCTCGTGACTGTGAAGCCATGTTACAAC
TACTGCTCAAACATCATGAGAGGCTGTTTGGCCAACCAAGGGGATCTCGATTTTGAATGGAA
CAATTTCATAGATGCTATGCTGATGGTGGCAGAGAGGCTAGAGGGTCCTTTCAACATTGAAT
CGGTCATGGATCCCATCGATGTGAAGATTTCTGATGCTATTATGAACATGCAGGATAATAGT
GTTCAAGTGTCTCAGAAGGTTTTCCAGGGATGTGGACCCCCCAAGCCCTCCAGCTGGACG
AATTTCTCGTTCCATCTCTGAAAGTGCCCTTCAGTGCTCGCTTCAGACCACATCACCCGAGG
AACGCCCAACCAAGCAAGCTGGCACTAGTTTGGACCGACTGGTTACTGATGTCAAGGAGAAA
CTGAAACAGGCCAAGAAATTTCTGGTCCCTCCCTTCCGAGCAACGTTTGCAACGATGAGAGGAT
GGCTGCAGGAAACGGCAATGAGGATGACTGTTGGAATGGGAAAGGCAAAAGCAGGTACCTGT
TTGCAGTGACAGGAAATGGATTAGCCAACCAAGGGCAACAACCCAGAGGTCCAGGTTGACACC
AGCAAACAGACATACTGATCCTTCGTCAAATCATGGCTCTTCGAGTGATGACCAGCAAGAT
GAAGAATGCATACAATGGGAACGACGTGGACTTCTTTGATATCAGTGATGAAAGTAGTGGAG
AAGGAAGTGGAAGTGGCTGTGAGTATCAGCAGTGCCCTTCAGAGTTTGACTACAAATGCCACT
GACCATGCTGGGAAGAGTGCCAATGAGAAAGCCGACAGTGCTGGTGTCCGTCTCGGGGCACA
GGCCTACCTCCTCACTGTCTTCTGCATCTTGTTCCTGGTTATGCAGAGAGAGTGGAGATAAT
TCTCAAACCTCTGAGAAAAAGTGTTCATCAAAAAGTTAAAAGGCACCAGTTATCACTTTTCTA
CCATCCTAGTGACTTTTGCTTTTAAATGAATGGACAACAATGTACAGTTTTTACTATGTGGC
CACTGGTTTAAAGAGTGCTGACTTTGTTTTCTCATTAGTTTTGGGAGGAAAAGGACTGTG
CATTGAGTTGGTTCTGCTCCCCCAAACCATGTTAAACGTGGCTAACAGTGATAGGTACAGAA
CTATAGTTAGTTGTGCATTTGTGATTTTATCACTCTATTATTTGTTTGTATGTTTTTTTCTC
ATTTCTGTTTGTGGGTTTTTTTTTCCAACGTGTGATCTCGCCTTGTTCCTTACAAGCAAACAG
GGTCCCTTCTTGGCACGTAACATGTACGTATTTCTGAAATATTAAATAGCTGTACAGAAGCA
GGTTTTATTTATCATGTTATCTTATTAAAAAGAAAAAGCCCAAAAGC

FIGURE 97

MARFGLPALLCTLAVLSAALLAELKSKSCSEVRRLYVSKGFNKNDAPLHEINGDHLKICPQ
GSTCCSQEMEEKYSLQSKDDFKSVVSEQCNHLQAVFASRYKKFDEFKELLENAEKSLNDMF
VKTYGHLYMQNSELFKDLFVELKRYVVGNVNLEMLNDFWARLLERMFRLVNSQYHFTDEY
LECVSKYTEQLKPFQDVPRKLLQVTRAFVAARTFAQGLAVAGDVVSKVSVVNPTAQCTHAL
LKMIYCSHCRGLVTVKPCYNYCSNIMRGCLANQGDLD FEWNNFIDAMLMVAERLEGPFNIES
VMDPIDVKISDAIMNMQDNSVQVSQKVFQCGPPKPLPAGRISRSISESAFSARFRPHHPEE
RPTTAAGTSLDRLVTDVKEKLQAKKFWSSLPSNVCNDERMAAGNGNEDDCWNGKGKSRYL
AVTGNGLANQGNNPEVQVDTSKPDILILRQIMALRVMTSKMKNAYNGNDVDFDISDESSGE
GSGSGCEYQQCPSEFDYNATDHAGKSANEKADSAGVRPGAQAYLLTVFCILFLVMQREWR

FIGURE 98

CTCGCCCTCAAATGGGAACGCTGGCCTGGGACTAAAGCATAGACCACCAGGCTGAGTATCCT
GACCTGAGTCATCCCCAGGGATCAGGAGCCTCCAGCAGGGAACCTTCCATTATATTCTTCAA
GCAACTTACAGCTGCACCGACAGTTGCGATGAAAGTTCTAATCTCTTCCCTCCTCCTGTTGC
TGCCACTAATGCTGATGTCCATGGTCTCTAGCAGCCTGAATCCAGGGGTCGCCAGAGGCCAC
AGGGACCGAGGCCAGGCTTCTAGGAGATGGCTCCAGGAAGGCGGCCAAGAATGTGAGTGCAA
AGATTGGTTCCTGAGAGCCCCGAGAAGAAAATTTCATGACAGTGTCTGGGCTGCCAAAGAAGC
AGTGCCCCCTGTGATCATTTCAAGGGCAATGTGAAGAAAACAAGACACCAAAGGCACCACAGA
AAGCCAAACAAGCATTCCAGAGCCTGCCAGCAATTTCTCAAACAATGTCAGCTAAGAAGCTT
TGCTCTGCCTTTGTAGGAGCTCTGAGCGCCCACTCTTCCAATTAAACATTCTCAGCCAAGAA
GACAGTGAGCACACCTACCAGACACTCTTCTTCTCCACCTCACTCTCCCACTGTACCCACC
CCTAAATCATTCCAGTGCTCTCAAAAAGCATGTTTTTCAAGATCATTTTGTGTTGCTCTC
TCTAGTGTCTTCTTCTCTCGTCAGTCTTAGCCTGTGCCCTCCCCTTACCCAGGCTTAGGCTT
AATTACCTGAAAGATTCCAGGAACTGTAGCTTCCTAGCTAGTGTCAATTAACCTTAAATGC
AATCAGGAAAGTAGCAAACAGAAGTCAATAAATATTTTTAAATGTCAAAAAAAAAAAAAAAAAA

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FIGURE 99

MKVLISLLLLLPLMLMSMVSSSLNPGVARGHRDRGQASRRWLQEGGQECECKDWFLRAPRR
KFMTVSGLPKKQCPDHFKGNVKKTRHQRHHRKPNKHSRACQQFLKQCQLRSFALPL

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FIGURE 100

AATGGCTGTCTTAGTACTTCGCCTGACAGTTGTCCTGGGACTGCTTGTCTTATTCTTGACCT
GCTATGCAGACGACAAACCAGACAAGCCAGACGACAAGCCAGACGACTCGGGCAAAGACCCA
AAGCCAGACTTCCCCAAATTCCTAAGCCTCCTGGGCACAGAGATCATTGAGAATGCAGTCGA
GTTTCATCCTCCGCTCCATGTCCAGGAGCACAGGATTTATGGAATTTGATGATAATGAAGGAA
AACATTTCATCAAAGTGACATCCTCAGGACACACCCATGTGGCTCCTGGACAATCCAAGAGCA
GCCAAATCCTGCTTTTCCAGTTTGGCTCCACAAGTCCTCCAGGACAGAGCCCTCAAAGCAAC
TCCCAACGAGTTCTCAGGATTCAGGCTCTGGCTTCAACCAAACAGAACTCATTTTGAACACC
CTGACTGCATTTTTGCTTTTAGAAAGTTAGAATAAATATGGCGCTTTGGGATCACATAGTTG
ATGGAGAGGAAA

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FIGURE 101

MAVLVLRRLTVVLGLLVLFLTCYADDKPKDPDDKPDGKDPKPDFPKFLSLLGTEIIENAVE
FILRSMRSTGFMEFDDNEGKHSSK

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FIGURE 102

GGACGCCAGCGCCTGCAGAGGCTGAGCAGGGAAAAAGCCAGTGCCCCAGCGGAAGCACAGCT
CAGAGCTGGTCTGCCATGGACATCCTGGTCCCCTCCTGCAGCTGCTGGTGCTGCTTCTTAC
CCTGCCCCCTGCACCTCATGGCTCTGCTGGGCTGCTGGCAGCCCCCTGTGCAAAAGCTACTTCC
CCTACCTGATGGCCGTGCTGACTCCCAAGAGCAACCGCAAGATGGAGAGCAAGAAACGGGAG
CTCTTCAGCCAGATAAAAGGGGCTTACAGGAGCCTCCGGGAAAGTGGCCCTACTGGAGCTGGG
CTGCGGAACCGGAGCCAACTTTAGTTCTACCCACCGGGCTGCAGGGTCACCTGCCTAGACC
CAAAATCCCCACTTTGAGAAGTTCCTGACAAAGAGCATGGCTGAGAACAGGCACCTCCAATAT
GAGCGGTTTGTGGTGGCTCCTGGAGAGGACATGAGACAGCTGGCTGATGGCTCCATGGATGT
GGTGGTCTGCACTCTGGTGCTGTGCTCTGTGCAGAGCCCAAGGAAGGTCCTGCAGGAGGTCC
GGAGAGTACTGAGACCGGGAGGTGTGCTCTTTTTCTGGGAGCATGTGGCAGAACCATATGGA
AGCTGGGCCTTCATGTGGCAGCAAGTTTTGAGCCCACTTGAAACACATTGGGGATGGCTG
CTGCCTCACCAGAGAGACCTGGAAGGATCTTGAGAACGCCCAGTTCTCCGAAATCCAAATGG
AACGACAGCCCCCTCCCTTGAAGTGGCTACCTGTTGGGCCCCACATCATGGGAAAGGCTGTC
AAACAATCTTTCCCAAGCTCCAAGGCACTCATTTGCTCCTTCCCCAGCCTCCAATTAGAACA
AGCCACCCACCAGCCTATCTATCTTCCACTGAGAGGGACCTAGCAGAATGAGAGAAGACATT
CATGTACCACCTACTAGTCCCTCTCTCCCCAACCTCTGCCAGGGCAATCTCTAACTTCAATC
CCGCCTTCGACAGTGAAAAAGCTCTACTTCTACGCTGACCCAGGGAGGAAACACTAGGACCC
TGTTGTATCCTCAACTGCAAGTTTCTGGACTAGTCTCCCAACGTTTGCCTCCCAATGTTGTC
CCTTTCCTTCGTTCCCATGGTAAAGCTCCTCTCGCTTTCCTCCTGAGGCTACACCCATGCGT
CTCTAGGAACCTGGTCACAAAAGTCATGGTGCCTGCATCCCTGCCAAGCCCCCTGACCCTCT
CTCCCCACTACCACCTTCTTCTGAGCTGGGGGCACCAGGGAGAATCAGAGATGCTGGGGAT
GCCAGAGCAAGACTCAAAGAGGCAGAGGTTTTGTTCTCAAATATTTTTTAATAAATAGACGA
AACCACG

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FIGURE 103

MDILVPLLQLLVLLLTLPPLHLMALLGCWQPLCKSYFPYLMAVLTPKSNRKMESKKRELFSQL
KGLTGASGKVALLELGCGTGANFQFYPPGCRVTCCLDPNPHFEKFLTKSMAENRHLQYERFVV
APGEDMRQLADGSMDVVVCTLVLCVQSPRKVLQEVRRVLRPGGVLEFFWEHVAEPYGSWAFM
WQQVFEPTWKHIGDGCCLTRETWKDLENAQFSEIQMERQPPPLKWLFPVGPHIMGKAVKQSF
SSKALICSFPSLQLEQATHQPIYLPLRGT

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FIGURE 104

GTGGGATTTATTTGAGTGCAAGATCGTTTTCTCAGTGGTGGTGGAAAGTTGCCTCATCGCAGG
CAGATGTTGGGGCTTTGTCCGAACAGCTCCCCCTCTGCCAGCTTCTGTAGATAAGGGTTAAAA
ACTAATATTTATATGACAGAAGAAAAAGATGTCATTCCGTAAAGTAAACATCATCATCTTGG
TCCTGGCTGTTGCTCTCTTCTTACTGGTTTTGCACCATAACTTCCTCAGCTTGAGCAGTTTTG
TTAAGGAATGAGGTTACAGATTGAGGAATTGTAGGGCCTCAACCTATAGACTTTGTCCCAAA
TGCTCTCCGACATGCAGTAGATGGGAGACAAGAGGAGATTCTGTGGTCATCGCTGCATCTG
AAGACAGGCTTGGGGGGGCCATTGCAGCTATAAACAGCATTGAGCACAACACTCGCTCCAAT
GTGATTTTCTACATTGTTACTCTCAACAATACAGCAGACCATCTCCGGTCTGGCTCAACAG
TGATTCCCTGAAAAGCATCAGATACAAAATTGTCAATTTTGACCCTAAACTTTTGGAAGGAA
AAGTAAAGGAGGATCCTGACCAGGGGAATCCATGAAACCTTTAACCTTTGCAAGGTTCTAC
TTGCCAATTCTGGTTCCCAGCGCAAAGAAGGCCATATACATGGATGATGATGTAATTGTGCA
AGGTGATATTCTTGCCCTTTACAATACAGCACTGAAGCCAGGACATGCAGCTGCATTTTCAG
AAGATTGTGATTGAGCCTCTACTAAAGTTGTCATCCGTGGAGCAGGAAACCAGTACAATTAC
ATTGGCTATCTTGACTATAAAAAGGAAAGAATTTCGTAAGCTTTCCATGAAAGCCAGCACTTG
CTCATTTAATCCTGGAGTTTTTTGTTGCAAACCTGACGGAATGGAAACGACAGAATATAACTA
ACCAACTGGAAAAATGGATGAAACTCAATGTAGAAGAGGGACTGTATAGCAGAACCTGGCT
GGTAGCATCACAACACCTCCTCTGCTTATCGTATTTTATCAACAGCACTCTACCATCGATCC
TATGTGGAATGTCCGCCACCTTGGTTCCAGTGCTGGAAAACGATATTCACCTCAGTTTGTA
AGGCTGCCAAGTTACTCCATTGGAATGGACATTTGAAGCCATGGGGAAGGACTGCTTCATAT
ACTGATGTTTGGGAAAAATGGTATATTCCAGACCCAACAGGCAAATTC AACCTAATCCGAAG
ATATACCGAGATCTCAAACATAAAGTGAAACAGAATTTGAACTGTAAGCAAGCATTCTCAG
GAAGTCCTGGAAGATAGCATGCATGGGAAGTAACAGTTGCTAGGCTTCAATGCCTATCGGTA
GCAAGCCATGGAAAAAGATGTGTGCTAGGTAAAGATGACAACTGCCCTGTCTGGCAGTC
AGCTTCCCAGACAGACTATAGACTATAAATATGTCTCCATCTGCCTTACCAAGTGTCTTCTT
ACTACAATGCTGAATGACTGGAAAGAAGAACTGATATGGCTAGTTCAGCTAGCTGGTACAGA
TAATTCAAAACTGCTGTTGGTTTTAATTTTGTAACCTGTGGCCTGATCTGTAAATAAACTT
ACATTTTTC

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FIGURE 105

MSFRKVNIIILVLAVALFLLVLHHNFLSLSSLRNEVTDSGIVGPQPIDFVPNALRHAVDGR
QEEIPVVIAASEQRLGGAIAAINS IQHNTRSNVIFYIVTLNNTADHLRSWLNSDSLKSIRYK
IVNFDPKLLEGKVKEDPDQGESMKPLTFARFYLPILVPSAKKAIYMDDDVIVQGDILALYNT
ALKPGHAAAFSEDCDSASTKV VIRGAGNQNYIGYLDYKKERIRKLSMKASTCSFNPGVFVA
NLTEWKRQNI TNQLEKWMKLNVEEGLYSRTL AGSITTPPLLIVFYQQHSTIDPMWNVRLGS
SAGKRYSPQFVKAALLHWNGHLKPWGRTASYTDVWEKWYIPDPTGKFNLIRRYTEISNIK

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FIGURE 106

TGGTTTTTGCCCCATAAATTCCTCAGCTTGAGCAGTTTGTTAAGGAATGAGGTTACAGATT
CAGGAATTNTAGGNCCTCAACCTNTAGANTTTGTCCCAAATGTTCTCCGACATGCAGTAGAT
GGGAGACAAGAGGAGATTCTGTGGTCATCGCTGCATNTGAAGACAGGCTTGGGGGGGCCAT
TGCAGCTATAAACAGCATTTCAGCACAACTCGNTCCAATGTGATTTTCTACATTGTTACTC
TCAACAATACAGCAGACCATNTCCGGTCTTGGNTCAACAGTGATTCCCTGAAAAGCATCAGA
TACAAAATTGTCAATTTTGACCCCTAACTTTTGGGAAGGAAAAGTAAAGGAGGATCCTGACCA
GGGGGAATCCATGAAACCTTTAACCTTTGCAAGGTTCTACTTGCCAATTCTGGTTCCCAGCG
CAAAGAAGGCCATATACATGGATGATGATGTAATTGTGCAAGGTGATATTCTTGCCCTTTAC
AATACAGCACTGAAGCCAGGACATGCAGCTGCATTTTCAGAAGATTGTGATTCAGCCTCTAC
TAAAGTTGTCATCCGTGGAGCAGGAAA

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FIGURE 107

CGACGCTCTAGCGGTTACCGCTGCGGGCTGGCTGGGCGTAGTGGGGCTGCGCGGCTGCCACG
GAGCTAGAGGGCAAGTGTGCTCGGCCCAGCGT3CAGGGAACGCGGGCGGCCAGACAACGGGC
TGGGCTCCGGGGCCTGCGGCGCGGGCGCTGAGCTGGCAGGGCGGGTCCGGGCGCGGGCTGCA
TCCGCATCTCCTCCATCGCCTGCAGTAAGGGCGGCCGCGGCGAGCCTTTGAGGGGAACGACT
TGTCCGAGCCCTAACCAGGGGTGTCTCTGAGCCTGGTGGGATCCCCGAGCGTCACATCACT
TTCCGATCACTTCAAAGTGGTTAAAACTAATATTTATATGACAGAAGAAAAAGATGTCATT
CCGTAAAGTAAACATCATCATCTTGGTCCTGGGCTGTTGCTCTCTTCTTACTGGTTTTGCAC
CATAACTTCCTCAGCTTGAGGCAGTTTGTAAAGGAATGAGGTTACAGATTGAGGAATTGTAG
GGCCTCAACCTATAGGACTTTGTCCCAAATGCTCTCCGACATGCAGTAGATGGGAGACAAGA
GGAGATTCTGTGGTCATCGCTGCATCTGAAGACAGGCTTGGGGGGGCCATTGCAGCTATAA
ACAGCATTGAGCACAACACTCGCTCCAATGTGATTTTCTACATTGTTACTCTCAACAATACA
GCAGACCATCTCCGGTCCTGGGCTCAACAGTGATTCCCTGAAAAGCATCAGATACAAAATTG
TCAATTTTGACCCCTAACTTTTGAAGGAAAAGTAAAGGAGGATCCTGACCAGGGGGAATCC
ATGAAACCTTTAACCTTTGCAAGGTTCTACTTGCCAATTCTGGGTTCCAGCGCAAAGAAGG
CCATATACATGGATGATGATGTAATTGTGCAAGGTGATATTCTTGCCCTTTACAATACAGCA
CTGAAGCCAGGACATGCAGCTGCATTTTCAGAAGATTGTGATTGAGCCTCTACTAAAGTTGT
CATCCGTGGAGCAGGAAACCAGTACAATTACATTGGCTATCTTGACTATAAAAAGGAAAGAA
TTCGTAAGCTTTCCATGAAAGCCAGCACTTGCTCATTTAATCCTGGAGTTTTTGTGTGCAAC
CTGACGGAATGGAAACGACAGAATATACTAACCAACTGGAAAAATGGATGAAACTCAATGT
AGAAGAGGGACTGTATAGCAGAACCCCTGGCTGGTAGCATCACAACACCTCCTCTGCTTATCG
TATTTTATCAACAGCACTCTACCATCGATCCTATGTGGAATGTCCGCCACCTTGGTTCCAGT
GCTGGAAAACGATATTCACCTCAGTTTGTAAAGGCTGCCAAGTTACTCCATTGGAATGGACA
TTTGAAGCCATGGGGAAGGACTGCTTCATATACTGATGTTTGGGGAAAAATGGTATATTCCA
GACCCAACAGGCAAATTCAACCTAATCCGAAGATATACCGAGATCTCAAACATAAAGTGAAA
CAGAATTTGAACTGTAAGCAAGCATTTCTCAGGAAGTCCTGGAAGATAGCATGCGTGGGAAG
TAACAGTTGCTAGGCTTCAATGCCTATCGGTAGCAAGCCATGGAAAAAGATGTGTCAGCTAG
GTAAAGATGACAACTGCCCTGTCTGGCAGTCAGCTTCCCAGACAGACTATAGACTATAAAT
ATGTCTCCATCTGCCTTACCAAGTGTCTTCTTACTACAATGCTGAATGACTGGAAAGAAGAA
CTGATATGGCTAGTTCAGCTAGCTGGTACAGATAATTCAAACTGCTGTTGGTTTTAATTTT
GTAACCTGTGGCCTGATCTGTAAATAAACTTACATTTTTCAATAGGTAAAAAAAAAAAAAA
AAAAAA

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FIGURE 108

CTGCAGGTAGACATCTCCACTGCCCAGGAATCACTGAGCGTGCAGACAGCACAGCCTCCTCT
GAAGGCCGGCCATACCAGAGTCCTGCCTCGGCATGGGCCTCACCATTGAGGCAGCTCCACTG
TCTGTGCTGGTCTGAGGGTGCTGCCTGTCAATGGGGGCAGCCATCTCCCAGGGGGCCCTCATC
GCCATCGTCTGCAACGGTCTCGTGGGCTTCTTGCTGCTGCTGCTCTGGGTCACTCCTCTGCTG
GGCCTGCCATTCTCGTCTGCCGACGTTGACTCTCTCTCTGAATCCAGTCCCAACTCCAGCCC
TGGCCCCCTGTCTGAGAAGGCCCCACCACCCAGAACCCAGCCATGAAGGCAGCTACCTGC
TGCAGCCCTGAAGGCCCCCTGGCCTAGCCTGGAGCCCAGGACCTAAGTCCACCTCACCTAGAG
CCTGGAATTAGGATCCCAGAGTTCAGCCAGCCTGGGGTCCAGAACTCAAGAGTCCGCCCTGCT
TGGAGCTGGACCCAGCGGCCCAGAGTCTAGCCAGCTTGGCTCCAATAGGAGCTCAGTGGCCC
TAAGGAGATGGGCCTGGGGTGGGGGCTTATGAGTTGGTGCTAGAGCCAGGGCCATCTGGACT
ATGCTCCATCCCAAGGGCCAAGGGTCAGGGGCCGGGTCCACTCTTTCCCTAGGCTGAGCACC
TCTAGGCCCTCTAGGTTGGGGAAGCAAACCTGGAACCCATGGCAATAATAGGAGGGTGTCCAG
GCTGGGGCCCTCCCCTGGTCCTCCAGTGTTTGCTGGATAATAAATGGAACCTATGGCTCTAA
AAAAAAAAAAAAAAAAAAAA

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FIGURE 109

MGAAISQGALIAIVCNGLVGFLLLLLWVILCWACHSRLPTLTLSLNPVPTPALAPVLRPHH

PRSPAMKAATCCSPEGPWPSLEPRT

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FIGURE 110

GTTTGAATTCCTTCAACTATACCCACAGTCCAAAAGCAGACTCACTGTGTCCCAGGCTACCA
GTTCCCTCCAAGCAAGTCATTTCCCTTATTTAACCGATGTGTCCCTCAAACACCTGAGTGCTA
CTCCCTATTTGCATCTGTTTTGATAAATGATGTTGACACCCTCCACCGAATTCTAAGTGGAA
TCATGTCGGAAGAGATACAATCCTTGGCCTGTGTATCCTCGCATTAGCCTTGTCTTTGGCC
ATGATGTTTACCTTCAGATTCATCACCACCCTTCTGGTTCACATTTTCATTTTATTGGTTAT
TTTGGGATTGTTGTTTGTCTGCGGTGTTTTATGGTGGCTGTATTATGACTATACCAACGACC
TCAGCATAGAATTGGACACAGAAAGGGAAAATATGAAGTGCCTGCTGGGGTTTGCTATCGTA
TCCACAGGCATCACGGCAGTGCTGCTCGTCTTGATTTTTGTTCTCAGAAAGAGAATAAAATT
GACAGTTGAGCTTTTCCAAATCACAAATAAAGCCATCAGCAGTGCTCCCTTCCTGCTGTTCC
AGCCACTGTGGACATTTGCCATCCTCATTTTCTTCTGGGTCCTCTGGGTGGCTGTGCTGCTG
AGCCTGGGAACTGCAGGAGCTGCCCAGGTTATGGAAGGCGGCCAAGTGAATATAAGCCCCCT
TTCGGGCATTTCGGTACATGTGGTTCGTACCATTTAATTGGCCTCATCTGGACTAGTGAATTCA
TCCTTGCGTGCCAGCAAATGACTATAGCTGGGGCAGTGGTTACTTGTTATTTCAACAGAAGT
AAAAATGATCCTCCTGATCATCCCATCCTTTTCGTCTCTCTCCATTCTCTTCTTCTACCATCA
AGGAACCGTTGTGAAAGGGTCATTTTAACTCTCTGTGGTGAGGATTCCGAGAATCATTGTCA
TGTACATGCAAAACGCACTGAAAGAACAGCAGCATGGTGCATTGTCCAGGTACCTGTTCCGA
TGCTGCTACTGCTGTTTTCTGGTGTCTTGACAAATACCTGCTCCATCTCAACCAGAATGCATA
TACTACAACCTGCTATTAAATGGGACAGATTTCTGTACATCAGCAAAAGATGCATTCAAAATCT
TGTCCAAGAACTCAAGTCACTTTACATCTATTAACTGCTTTGGGAGACTTCATAATTTTTCTA
GGAAAGGTGTTAGTGGTGTGTTTCACTGTTTTTGGAGGACTCATGGCTTTTAACTACAATCG
GGCATTCCAGGTGTGGGCAGTCCCTCTGTTATTGGTAGCTTTTTTTGCCTACTTAGTAGCCC
ATAGTTTTTTATCTGTGTTTGAAACTGTGCTGGATGCACTTTTCCTGTGTTTTGCTGTTGAT
CTGGAAACAAATGATGGATCGTCAGAAAAGCCCTACTTTATGGATCAAGAATTTCTGAGTTT
CGTAAAAGGAGCAACAAATTAAACAATGCAAGGGCACAGCAGGACAAGCACTCATTAAGGA
ATGAGGAGGGAACAGAACTCCAGGCCATTGTGAGATAGATACCCATTTAGGTATCTGTACCT
GGAAAACATTTCCCTTCTAAGAGCCATTTACAGAATAGAAGATGAGACCACTAGAGAAAAGTT
AGTGAATTTTTTTTTAAAAGACCTAATAAACCCATTCTTCCTCAAAA

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FIGURE 111

MSGRDTILGLCILALALSLAMMFTFRFITLLVHIFISLVILGLLFVCGVLWWLYDYDTNDL
SIELDTERENMKCVLGFAIVSTGITAVLLVLIFVLRKRIKLTVELFQITNKAISSAPFLLFQ
PLWTFAILIFFWVLWVAVLLSLGTAGAAQVMEGGQVEYKPLSGIRYMWSYHLIGLIWTSEFI
LACQQMTIAGAVVTCYFNRSKNDPPDHPILSSLSILFFYHQGTVVKGSFLISVVRIPRIIVM
YMQNALKEQQHGALSRYLFRCCYCCFWCLDKYLLHLNQNAYTTTAINGTDFCTSAKDAFKIL
SKNSSHFTSINCFGDFIIFLGKVLVVCFTVFGGLMAFNYNRAFQVWAVPLLLVAFFAYLVAH
SFLSVFETVLDALFLCFAVDLETNDGSSEKPYFMDQEFLSFVKRSNKLNNARAQQDKHSLRN
EEGTELQAIVR

FIGURE 113

MRTVVLTMKASVIEMFLVLLVTGVHSNKETAKKIKRPKFTVPQINCDVKAGKIIDPEFIVKC
PAGCQDPKYHVYGTDVYASYSSVCGAAVHSGVLDNSGGKILVRKVAGQSGYKGSYSNGVQSL
SLPRWRESFIVLESKPKKGVITYPSALTYSSSKSPAAQAGETTKAYQRPPIPGTTAQPVILMQ
LLAVTVAVATPTTLPRPSPSAASTTIPRPQSVGHRSQEMDLWSTATYTTSSQNRPRADPGIQ
RQDPGAAAFQKPVGADVSLGLVPKEELSTQSLEPVSLGDPNCKIDLSFLIDGSTSIGKRRFR
IQKQLLADVAQALDIGPAGPLMGVVQYGDNPATHFNLKTHTNRDLKTAIEKITQRGGLSNV
GRAISFVTKNFFSKANGNRSGAPNVVVVMVDGWPTDKVEEASRLARESGINIFFITIEGAAE
NEKQYVVEPNFANKAVCRTNGFYSLHVQSWFGLHKTLLQPLVKRVCDTDRILACSKTCLNSADI
GFVIDGSSSVGTGNFRTVLQFVTNLTKFEISDTRIGAVQYTYEQRLFEFGFDKYSSKPDIL
LNAIKRVGYWSGGTSTGAAINFALQFLFKSKPNKRKLMILITDGRSYDDVRIPAMAAHLKG
VITYAIGVAWAAQEELEVIATHPARHDSFFVDEFNLHQYVPRIIQNICTEFNSQPRN

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FIGURE 114

CAGGATGAACTGGTTGCAGTGGCTGCTGCTGCTGCGGGGGCGCTGAGAGGACACGAGCTCTA
TGCCCTTTCCGGCTGCTCATCCCGCTCGGCCTCCTGTGCGCGCTGCTGCCCTCAGCACCATGGT
GCGCCAGGTCCCGACGGCTCCGCGCCAGATCCCGCCCACTACAGTTTTTCTCTGACTCTAAT
TGATGCACTGGACACCTTGCTGATTTTGGGGAATGTCTCAGAATTCCAAAGAGTGGTTGAAG
TGCTCCAGGACAGCGTGGACTTTGATATTGATGTGAACGCCTCTGTGTTTGAACAAACATT
CGAGTGGTAGGAGGACTCCTGTCTGCTCATCTGCTCTCCAAGAAGGCTGGGGTGGAAGTAGA
GGCTGGATGGCCCTGTTCCGGGCCTCTCCTGAGAAATGGCTGAGGAGGCGGCCCCGAAACTCC
TCCCAGCCTTTCAGACCCCCACTGGCATGCCATATGGAACAGTGAACCTTACTTCATGGCGTG
AACCCAGGAGAGACCCCTGTACCTGTACGGCAGGGATTGGGACCTTCATTGTTGAATTTGC
CACCTGAGCAGCCTCACTGGTGACCCGGTGTTTGAAGATGTGGCCAGAGTGGCTTTGATGC
GCCTCTGGGAGAGCCGGTCAGATATCGGGCTGGTCGGCAACCACATTGATGTGCTCACTGGC
AAGTGGGTGGCCAGGACGCAGGCATCGGGCTGGCGTGGACTCCTACTTTGAGTACTTGGT
GAAAGGAGCCATCCTGCTTCAGGATAAGAAGCTCATGGCCATGTTCTAGAGTATAACAAAG
CCATCCGGAACCTACACCCGCTTCGATGACTGGTACCTGTGGGTTCAGATGTACAAGGGGACT
GTGTCCATGCCAGTCTTCCAGTCTTGGAGGCCTACTGGCCTGGTCTTCAGAGCCTCATTGG
AGACATTGACAATGCCATGAGGACCTTCCTCAACTACTACACTGTATGGAAGCAGTTTGGGG
GGCTCCCGGAATTCTACAACATTCCTCAGGGATACACAGTGGAGAAGCGAGAGGGCTACCCA
CTTCGGCCAGAATTATTGAAAGCGCAATGTACCTCTACCGTGCCACGGGGGATCCCACCCT
CCTAGAACTCGGAAGAGATGCTGTGGAATCCATTGAAAAAATCAGCAAGGTGGAGTGC GGAT
TTGCAACAATCAAAGATCTGCGAGACCACAAGCTGGACAACCGCATGGAGTCGTTCTTCCTG
GCCGAGACTGTGAAATACCTCTACCTCCTGTTTGACCCAACCAACTTCATCCACAACAATGG
GTCCACCTTCGACGCGGTGATCACCCCTATGGGGAGTGCATCCTGGGGGCTGGGGGTACA
TCTTCAACACAGAAGCTCACCCCATCGACCTTGCCGCCCTGCACTGCTGCCAGAGGCTGAAG
GAAGAGCAGTGGGAGGTGGAGGACTTGATGAGGGAATTCTACTCTCTCAAACGGAGCAGGTC
GAAATTTCAGAAAAACACTGTTAGTTTCGGGGCCATGGGAACCTCCAGCAAGGCCAGGAACAC
TCTTCTCACCAGAAAACCATGACCAGGCAAGGGAGAGGAAGCCTGCCAAACAGAAGGTCCCA
CTTCTCAGCTGCCCCAGTCAGCCCTTCACCTCCAAGTTGGCATTACTGGGACAGGTTTTCTT
AGACTCCTCATAAACCCTGGATAATTTTTTTATTTTTATTTTTTTGAGGCTAAACTATAATA
AATTGCTTTTGGCTATCATAAAA

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FIGURE 115

MPFRLLIPLGLLCALLPQHGGAPGPDGSAPDPAHYSFSLTLIDALDTLLILGNVSEFQRVVE
VLQDSVDFDIDVNASVFETNIRVVGGLLSAHLSSKKAGVEVEAGWPCSGPLLRMAEEAARKL
LPAFQTPTGMPYGTVNLLHGVNPGETPVTCTAGIGTFIVEFATLSSLTGDPVFEDVARVALM
RLWESRSDIGLVGNHIDVLTGKWVAQDAGIGAGVDSYFEYLVKGAILLQDKKLMAMFLEYNK
AIRNYTRFDDWYLVWQMYKGTVSMPVFSLEAYWPGQLSLIGDIDNAMRTFLNYYTVWKQFG
GLPEFYNI PQGYTVEKREGYPLRPELIESAMYLYRATGDPPTLLELGRDAVESIEKISKVECG
FATIKDLRDHKL DNRMESFFLAETVKYLYLLFDPTNF IHNNGSTFDAVITPYGECILGAGGY
IFNTEAHPIDLAALHCCQRLKEEQWEVEDLMREFYSLKRSRSKFQKNTVSSGPWEPPARPGT
LFSPENHDQARERKPAKQKVPLLSCPSPQFTSKLALLGQVFLDSS

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FIGURE 116

AAAGTTACATTTTCTCTGGAACCTCTCCTAGGCCACTCCCTGCTGATGCAACATCTGGGTTTG
GGCAGAAAGGAGGGTGCTTCGGAGCCCCGCCCTTTCTGAGCTTCCTGGGCCGGCTCTAGAAACA
ATTCAGGCTTCGCTGCGACTCAGACCTCAGCTCCAACATATGCATTCTGAAGAAAGATGGCT
GAGATGGACAGAATGCTTTATTTTGGAAAGAAACAATGTTCTAGGTCAAACCTGAGTCTACCA
AATGCAGACTTTCACAATGGTTCTAGAAGAAATCTGGACAAGTCTTTTCATGTGGTTTTCT
ACGCATTGATTCCATGTTTGCTCACAGATGAAGTGGCCATTCTGCCTGCCCCCTCAGAACCTC
TCTGTACTCTCAACCAACATGAAGCATCTCTTGATGTGGAGCCCAGTGATCGCGCCTGGAGA
AACAGTGTAATACTGTCGAATACCAGGGGGAGTACGAGAGCCTGTACACGAGCCACATCT
GGATCCCCAGCAGCTGGTGCTCACTCACTGAAGGTCTTGAGTGTGATGTCACTGATGACATC
ACGGCCACTGTGCCATACAACCTTCGTGTCAGGGCCACATTGGGCTCACAGACCTCAGCCTG
GAGCATCCTGAAGCATCCCTTTAATAGAACTCAACCATCCTTACCCGACCTGGGATGGAGA
TCACCAAAGATGGCTTCCACCTGGTTATTGAGCTGGAGGACCTGGGGCCCCAGTTTGAGTTC
CTTGTTGGCCTACTGGAGGAGGGAGCCTGGTGCCGAGGAACATGTCAAAATGGTGAGGAGTGG
GGGTATTCCAGTGCACTTAGAAACCATGGAGCCAGGGGCTGCATACTGTGTGAAGGCCCAGA
CATTCGTGAAGGCCATTGGGAGGTACAGCGCCTTCAGCCAGACAGAATGTGTGGAGGTGCAA
GGAGAGGCCATTCCCCTGGTACTGGCCCTGTTTGCTTTGCTTTGCTTTCATGCTGATCCTTGT
GGTCGTGCCACTGTTTCGTCTGGAATGGGCCGGCTGCTCCAGTACTCCTGTTGCCCGTGG
TGGTCTCCAGACACCTTGAAAATAACCAATTCACCCAGAAAGTTAATCAGCTGCAGAAGG
GAGGAGGTGGATGCCTGTGCCACGGCTGTGATGTCTCCTGAGGAACTCCTCAGGGCCTGGAT
CTCATAGGTTTGCAGGAAGGGCCCAGGTGAAGCCGAGAACCTGGTCTGCATGACATGGAAACC
ATGAGGGGACAAGTTGTGTTTTCTGTTTTCCGCCACGGACAAGGGATGAGAGAAGTAGGAAGA
GCCTGTTGTCTACAAGTCTAGAAGCAACCATCAGAGGCAGGGTGGTTTGTCTAACAGAACAC
TGACTGAGGCTTAGGGGATGTGACCTCTAGACTGGGGGCTGCCACTTGCTGGCTGAGCAACC
CTGGGAAAAGTGACTTCATCCCTTCGGTCCTAAGTTTTCTCATCTGTAATGGGGGAATTACC
TACACACCTGCTAAACACACACACAGAGTCTCTCTATATATACACACGTACACATAAA
TACACCCAGCACTTGCAAGGCTAGAGGGAACTGGTGACACTCTACAGTCTGACTGATTGAG
TGTTTCTGGAGAGCAGGACATAAATGTATGATGAGAATGATCAAGGACTCTACACACTGGGT
GGCTTGGAGAGCCCACTTTCCAGAAATAATCCTTGAGAGAAAAGGAATCATGGGAGCAATGG
TGTTGAGTTCACTTCAAGCCCAATGCCGGTGACAGAGGGGAATGGCTTAGCGAGCTCTACAGT
AGGTGACCTGGAGGAAGGTACAGCCACACTGAAAATGGGATGTGCATGAACACGGAGGATC
CATGAACTACTGTAAAGTGTGACAGTGTGTGCACACTGCAGACAGCAGGTGAAATGTATGT
GTGCAATGCGACGAGAATGCAGAAGTCAGTAACATGTGCATGTTTGTGTGCTCCTTTTTTC
TGTTGGTAAAGTACAGAATTGAGCAATAAAAAGGGCCACCCTGGCCAAAAGCGGTAAAAAA
AAAAAAAAA

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FIGURE 117

MQTFTMVLEEIWTSLSFMWFFYALIPCLLTDEVAILPAPQNLSVLSTNMKHELLMWSPVIAPGE
TVYYSVEYQGEYESLYTSHIWIPSSWCSLTEGPECDDITATVPYNLRVRATLGSQTS
SILKHPFNRNSTILTRPGMEITKDGFLVIELEDLGPQFEFLVAYWRREPGAEEHVKMVRSG
GIPVHLETMEPGAAYCVKAQTFVKAIGRYSAFSQTECVQGEAIPLVLALFAFVGFMILIV
VVPLFVWKMGRLLQYSCCPVVVLPDTLKITNSPQKLISCRREEVDACATAVMSPEELLRAWIS

Important features:

Signal peptide:

amino acids 1-29

Transmembrane domain:

amino acids 230-255

N-glycosylation sites.

amino acids 40-43 and 134-137

Tissue factor proteins homology.

amino acids 92-119

Integrins alpha chain protein homology.

amino acids 232-262

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FIGURE 118

TCCTGCTGATGCACATCTGGGTTTGGCAAAGGAGGTTGCTTCGAGCCGCCCTTTCTAGCTT
CCTGGCCGGCTCTAGAACAATTGAGGCTTCGCTGCGACTAGACCTCAGCTCCAACATATGCA
TTCTGAAGAAAGATGGCTGAGATGACAGAATGCTTTATTTTGGAAAGAAACAATGTTCTAGG
TCAAACCTGAGTCTACCAAATGCAGACTTTCACAATGGTTCTAGAAGAAATCTGGACAAGTCT
TTTCATGTGGTTTTTCTACGCATTGATTCCATGTTTGCTCACAGATGAAGTGGCCATTCTGC
CTGCCCCCTCAGAACCTCTCTGTACTCTCAACCAACATGAAGCATCTCTTGATGTGGAGCCCA
GTGATCGCGCCTGGAGAAACAGTGTACTATTCTGTGCAATACCAGGGGGAGTACGAGAGCCT
GTACACGAGCCACATCTGGATCCCCAGCAGCTGGTGCTCACTCACTGAAGGTCCTGAGTGTG
ATGTCACTGATGACATCACGGCCACTGTGCCATACAACCTTTGTGTGAGGGCCACATTGGGC
TCACAGACCTCAGCCTGGAGCATCCTGAAGCATCCCTTTAATAGAAACTCAACCATCCTTAC
CCGACCTGGGATGGAGATCACCAAAGATGGCTTNCACCTGGTTATTGAGCTGGAGGACCTGG
GGCCCCAGTTTGAGTTCCTTGTGGCCTANTGGAGGAGGGGCGAACCCCTTGCGGCGCAAGGG
GTTNGCGAACCCCTTGCGGCCGCTGGGGTATCTCTCGAGAAAAGAGAGGCCCAATATGACCCAC
ATACTCAATATGGACGAANTGCTATTGTCCACCTGTTTGAGTGGCGCTGGGTTGAT

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FIGURE 119

CGGACGCGTGGGCGGCCACCTCCGGAACAAGCCATGGTGGCGGCGACGGTGGCAGCGGCGTG
GCTGCTCCTGTGGGCTGCGGCCTGCGCGCAGCAGGAGCAGGACTTCTACGACTTCAAGGCGG
TCAACATCCGGGGCAAACCTGGTGTGCTGGAGAAGTACCGCGGATCGGTGTCCCTGGTGGTG
AATGTGGCCAGCGAGTGC GGCTTCACAGACCAGCACTACCGAGCCCTGCAGCAGCTGCAGCG
AGACCTGGGCCCCCACCCTTTAACGTGCTCGCCTTCCCCTGCAACCAGTTTGGCCAACAGG
AGCCTGACAGCAACAAGGAGATTGAGAGCTTTGCCCGCCGCACCTACAGTGTCTCATTCCCC
ATGTTTAGCAAGATTGCAGTCACCGGTACTGGTGCCCATCCTGCCTTCAAGTACCTGGCCCA
GACTTCTGGGAAGGAGCCCACCTGGAACCTTCTGGAAGTACCTAGTAGCCCCAGATGGAAGG
TGGTAGGGGCTTGGGACCCAACTGTGTCAGTGGAGGAGGTCAGACCCAGATCACAGCGCTC
GTGAGGAAGCTCATCCTACTGAAGCGAGAAGACTTATAAACCACCGCTCTCCTCCTCCACCA
CCTCATCCCGCCCACCTGTGTGGGGCTGACCAATGCAAACCTCAAATGGTGCTTCAAAGGGAG
AGACCCACTGACTCTCCTTCCTTTACTCTTATGCCATTGGTCCCATCATTCTTGTGGGGGAA
AAATTCTAGTATTTTGATTATTTGAATCTTACAGCAACAAATAGGAACTCCTGGCCAATGAG
AGCTCTTGACCAGTGAATCACCAGCCGATACGAACGTCTTGCCAACAAAAATGTGTGGCAA
TAGAAGTATATCAAGCAATAATCTCCCACCCAAGGCTTCTGTAAACTGGGACCAATGATTAC
CTCATAGGGCTGTTGTGAGGATTAGGATGAAATACCTGTGAAAGTGCCTAGGCAGTGCCAGC
CAAATAGGAGGCATTCAATGAACATTTTTTGCATATAAACCAAAAAATAACTTGTATCAAT
AAAACTTGCAATCCAACATGAATTTCCAGCCGATGATAATCCAGGCCAAAGGTTTAGTTGTT
GTTATTTCTCTGTATTATTTCTTCATTACAAAAGAAATGCAAGTTCATTGTAACAATCCA
AACAAATACCTCACGATATAAAATAAAAAATGAAAGTATCCTCCTCAAAAA

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FIGURE 120

MVAATVAAAWLLLWAAACAQQEQDFYDFKAVNIRGKLVSLEKYRGSVSLVNVASECGFTDQ
HYRALQQQLQRDLGPHHFNVLAFFPCNQFGQQEPDSNKEIESFARRTYSVSFPMFSKIAVTGTG
AHPAFKYLAQTSGKEPTWNFWKYL VAPDGKVVGAWDPTVSVEEVRPQITALVRKLILLKREDL

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FIGURE 121

CGGACGCGTGGGCGGGCCGGGACGCAGGGCAAAGCGAGCCATGGCTGTCTACGTCGGGATGC
TGCGCCTGGGGAGGCTGTGCGCCGGGAGCTCGGGGGTGCTGGGGGCCCGGGCGCCCTCTCT
CGGAGTTGGCAGGAAGCCAGGTTGCAGGGTGTCCGCTTCCTCAGTTCCAGAGAGGTGGATCG
CATGGTCTCCACGCCCATCGGAGGCCTCAGCTACGTTTCAGGGGTGCACCAAAAAGCATCTTA
ACAGCAAGACTGTGGGCCAGTGCTTGAGACCACAGCACAGAGGGTCCCAGAACGAGAGGGCC
TTGGTCGTCTCCATGAAGACGTCAGGTTGACCTTTGCCCAACTCAAGGAGGAGGTGGACAA
AGCTGCTTCTGGCCTCCTGAGCATTGGCCCTTGCAAAGGTGACCGGCTGGGCATGTGGGGAC
CTAACTCCTATGCATGGGTGCTCATGCAGTTGGCCACCGCCAGGCGGGCATATTCTGGTG
TCTGTGAACCCAGCCTACCAGGCTATGGAAGTGGAGTATGTCTCAAGAAGGTGGGCTGCAA
GGCCCTTGTTTCCCAAGCAATTCAAGACCCAGCAATACTACAACGTCCTGAAGCAGATCT
GTCCAGAAGTGGAGAATGCCAGCCAGGGGCCCTGAAGAGTCAGAGGCTCCCAGATCTGACC
ACAGTCATCTCGGTGGATGCCCCCTTTGCCGGGGACCCCTGCTCCTGGATGAAGTGGTGGCGGC
TGGCAGCACACGGCAGCATCTGGACCAGCTCCAATACAACCAGCAGTTCTGTCTCTGCCATG
ACCCCATCAACATCCAGTTCACCTCGGGGACAACAGGCAGCCCCAAGGGGGCCACCCTCTCC
CACTACAACATTGTCAACAACCTCAACATTTTAGGAGAGCGCCTGAAACTGCATGAGAAGAC
ACCAGAGCAGTTGCGGATGATCCTGCCCAACCCCTGTACCATTGCCCTGGGTTCCTGGGCAG
GCACAATGATGTGTCTGATGTACGGTGCCACCCTCATCCTGGCCTCTCCCATCTTCAATGGC
AAGAAGGCACCTGGAGGCCATCAGCAGAGAGAGAGGCACCTTCCTGTATGGTACCCCCACGAT
GTTCTGTGGACATTCTGAACCAGCCAGACTTCTCCAGTTATGACATCTCGACCATGTGTGGAG
GTGTCAATTGCTGGGTCCCCTGCACCTCCAGAGTTGATCCGAGCCATCATCAACAAGATAAAT
ATGAAGGACCTGGTGGTTGCTTATGGAACCACAGAGAACAGTCCCGTGACATTCGCGCACTT
CCCTGAGGACACTGTGGAGCAGAAGGCAGAAAGCGTGGGCAGAAATTATGCCTCACACGGAGG
CCCGGATCATGAACATGGAGGCAGGGACGCTGGCAAAGCTGAACACGCCCGGGGAGCTGTGC
ATCCGAGGGTACTGCGTCATGCTGGGCTACTGGGGTGAGCCTCAGAAGACAGAGGAAGCAGT
GGATCAGGACAAGTGGTATTGGACAGGAGATGTGCCACAATGAATGAGCAGGGCTTCTGCA
AGATCGTGGGCCGCTCTAAGGATATGATCATCCGGGGTGGTGAGAACATCTACCCGCAGAG
CTCGAGGACTTCTTTCACACACACCCGAAGGTGCAGGAAGTGCAGGTGGTGGGAGTGAAGGA
CGATCGGATGGGGGAAGAGATTTGTGCCTGCATTCCGCTGAAGGACGGGGAGGAGACCACGG
TGGAGGAGATAAAAGCTTTCTGCAAAGGGAAGATCTCTCACTTCAAGATTCGGAAGTACATC
GTGTTTGTCAAAACTACCCCTCACCATTTTCAGGAAAGATCCAGAAATTCAAACCTTCGAGA
GCAGATGGAACGACATCTAAATCTGTGAATAAAGCAGCAGGCCTGTCTGGCCGGTTGGCTT
GACTCTCTCCTGTGAGAATGCAACCTGGCTTTATGCACCTAGATGTCCCAGCACCCAGTTT
TGAGCCAGGCACATCAAATGTCAAGGAATTGACTGAACGAACTAAGAGCTCCTGGATGGGTC
CGGGAACTCGCCTGGGCACAAGGTGCCAAAAGGCAGGCAGCCTGCCAGGCCCTCCCTCCTG
TCCATCCCCACATTCCCCTGTCTGTCTTGTGATTTGGCATAAAGAGCTTCTGTTTTCTTT
GAAAAAAAAAAAAAAAAA

FIGURE 122

MAVYVGMLRLGRLCAGSSGVLGARAALSRWQEARLQGVRFLSSREVD RMVSTPIGGLSYVQ
GCTKKHLNSKTVGQCLETTAQRVPEREALVVLHEDVRLTFAQLKEEVDKAASGLLSIGLCKG
DRLGMWGPN SYAWVLMQLATAQAGIILVSVNPAYQAMELEYVLKKVGCKALVFPKQFKTQQY
YNVLKQICPEVENAQPGALKSQRLPDLTTVISVDAPLPGTLLLDEVVAAGSTRQHLDQLQYN
QQFLSCHDPINIQFTSGTTGSPKGATLSHYNIVNNSNILGERLKLHEKTPEQLRMILPNPLY
HCLGSVAGTMMCLMYGATLILASPIFNGKKALEAISRERGTFLYGTPTMFVDILNQPDFSSY
DISTMCGGVIAGSPAPPELIRAIINKINMKDLVVAYGTTENSPVTFAHFPEDTVEQKAESVG
RIMPHTEARIMNMEAGTLAKLNTPGELCIRGYCVMLGYWGEPQKTEEAVDQDKWYWTGDVAT
MNEQGFCKIVGRSKDMIIRGGENIYPAELEDFHHTHPKVQEVQVVGVKDDRMGEEICACIRL
KDGEETTVEEIKAFCKGKISHFKIPKYIVFVTNYPLTISGKIQFKLREQMERHLNL

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FIGURE 123

CAACTCCAACATTTTAGGAGAGCGCCTGAAACTGCATGAGAAGACACCAGAGCAGTTGCGGA
TGATCCTGCCCCAACCCCTGTACCATTCGCTGGGTTCCGTGGCAGGCACAATGATGTGTCTG
ATGTACGGTGCCACCCTCATCCTGGCCTCTCCCATCTTCAATGGCAAGAAGGCACTGGAGGC
CATCAGCAGAGAGAGAGAGGCACCTTCCTGTATGGTACCCCCACGATGTTTCGTGGACATTCTGA
ACCAGCCAGACTTCTCCAGTTATGACATCTCGACCATGTGTGGAGGTGTCATTGCTGGGTCC
CCTGCACCTCCAGAGTTGATCCGAGCCATCATCAACAAGATAAATATGAAGGACCTGGTGGT
TGCTTATGGAACCACAGAGAACAGTCCCGTGACATTCGCGCACTTCCCTGAGGACACTGTGG
AGCAGAAGGCAGAAAGCGTGGGCAGAATTATGCCTCACACGGAGGCGCGGATCATGAACATG
GAGGCAGGGACGCTGGCAAAGCTGAACACGCCCGGGGAGCTGTGCATCCGAGGGTACTGCGT
CATGCTGGGCTACTGGGGTGAGCCTCAGAAGACAGAGGAAGCAGTGGATCAGGACAAGTGGT
ATTGGACAGGAGATGTCGCCAC

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FIGURE 124

GAGCAGGACGGAGCCATGGACCCCGCCAGGAAAGCAGGTGCCAGGCCATGATCTGGACTGC
AGGCTGGCTGCTGCTGCTGCTGCTTCGCGGAGGAGCGCAGGCCCTGGAGTGCTACAGCTGCG
TGCAGAAAGCAGATGACGGATGCTCCCCGAACAAGATGAAGACAGTGAAGTGCGCGCCGGGC
GTGGACGTCTGCACCGAGGCCGTGGGGGCGGTGGAGACCATCCACGGACAATTCTCGCTGGC
AGTGCGGGGTTGCGGTTCTGGGACTCCCCGGCAAGAATGACCGCGGCCTGGATCTTCACGGGC
TTCTGGCGTTCATCCAGCTGCAGCAATGCGCTCAGGATCGCTGCAACGCCAAGCTCAACCTC
ACCTCGCGGGCGCTCGACCCGGCAGGTAATGAGAGTGCATACCCGCCCCAACGGCGTGGAGTG
CTACAGCTGTGTGGGCCTGAGCCGGGAGGCGTGCCAGGGTACATCGCCGCGCGGTGCTGAGCT
GCTACAACGCCAGCGATCATGTCTACAAGGGCTGCTTCGACGGCAACGTACCTTGACGGCA
GCTAATGTGACTGTGTCCTTGCCCTGTCCGGGGCTGTGTCCAGGATGAATTCTGCACTCGGGA
TGGAGTAACAGGCCCAGGGTTCACGCTCAGTGGCTCCTGTTGCCAGGGGTCCCGCTGTAAC
CTGACCTCCGCAACAAGACCTACTTCTCCCCCTCGAATCCCACCCCTTGTCGGGCTGCCCCCT
CCAGAGCCCACGACTGTGGCCTCAACCACATCTGTCACCACTTCTACCTCGGCCCCAGTGAG
ACCCACATCCACCACCAACCCATGCCAGCGCCAACCAGTCAGACTCCGAGACAGGGAGTAG
AACACGAGGCCTCCCGGGATGAGGAGCCCAGGTTGACTGGAGGCGCCGCTGGCCACCAGGAC
CGCAGCAATTCAGGGCAGTATCCTGCAAAAGGGGGCCCCAGCAGCCCCATAATAAAGGCTG
TGTGGCTCCACAGCTGGATTGGCAGCCCTTCTGTTGGCCGTGGCTGCTGGTGTCTACTGT
GAGCTTCTCCACCTGGAAATTTCCCTCTCACCTACTTCTCTGGCCCTGGGTACCCCTCTTCT
CATCACTTCTGTTCCACCACTGGACTGGGCTGGGCCAGCCCCTGTTTTTCCAACATTCCC
CAGTATCCCCAGCTTCTGCTGCGCTGGTTTTCGGCTTTGGGAAATAAAATACCGTTGTATAT
ATTCTGCCAGGGGTGTTCTAGCTTTTTTGAGGACAGCTCCTGTATCCTTCTCATCCTTGTCTC
TCCGCTTGTCCTCTTGTGATGTTAGGACAGAGTGAGAGAAGTCAGCTGTACGGGGAAGGTG
AGAGAGAGGATGCTAAGCTTCCTACTCACTTTCTCCTAGCCAGCCTGGACTTTGGAGCGTGG
GGTGGGTGGGACAATGGCTCCCCACTCTAAGCACTGCCTCCCCTACTCCCCGCATCTTTGGG
GAATCGGTTCCCATATGTCTTCCTTACTAGACTGTGAGCTCCTCGAGGGGGGGCCCGGTAC
CCAATTCGCCCTATAGTGAGTCGTA

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FIGURE 125

MDPARKAGAQAAMIWTAGWLLLLLLRGGQALECYSCVQKADDGCSPNKMKTVKCAPGVDVCT
EAVGAVETIHGQFSLAVRGCGSGLPGKNDRGLDLHGLLAFIQLQQCAQDRCNALNLTSRAL
DPAGNESAYPPNGVECYSCVGLSREACQGTSPPVVSCYNASDHVYKGCDFGNVTLTAANVTV
SLPVRGCVQDEFCTRDGVTGPGFTLSGSCCQGSRCNSDLRNKTYFSPRIPPLVRLPPPEPTT
VASTTSVTTSTTSAPVRPTSTTKPMPAPTSQTPRQGVHEASRDEEPRLTGGAAGHQDRSNSG
QYPAKGGPQQPHNKGCVAPTAGLAALLLAVAAGVLL

[illegible]

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FIGURE 127

MELVLVFLCSLLAPMVLASAAEKEKEMDPFHYDYQTLRIGGLVFAVVLFSVGILLILSRCK
CSFNQKPRAPGDDEEAQVENLITANATEPQKQRTQVQPSGGSLWNLRRLLLEPLDANVDA

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FIGURE 128

AAACTTGACGCCATGAAGATCCCGGTCCTTCCTGCCGTGGTGCTCCTCTCCCTCCTGGTGCT
CCTCTGCCCAGGGAGCCACCCTGGGTGGTCCTGAGGAAGAAAGCACCATTGAGAATTATG
CGTCACGACCCGAGGCCTTTAACACCCCGTTCCTGAACATCGACAAATTGCGATCTGCGTTT
AAGGCTGATGAGTTCCTGAACTGGCAGCCCTCTTTGAGTCTATCAAAGGAAACTTCCTTT
CCTCAACTGGGATGCCTTTCCTAAGCTGAAAGGACTGAGGAGCGCAACTCCTGATGCCAGT
GACCATGACCTCCACTGGAAGAGGGGGCTAGCGTGAGCGCTGATTCTCAACCTACCATAACT
CTTTCCTGCCTCAGGAACTCCAATAAAACATTTTCCATCCAAA

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FIGURE 129

MKIPVLPVAVLLSLLVLHSAQGATLGGPEEESTIENYASRPEAFNTPFLNIDKLRSFAKDE
FLNWHALFESIKRKLPFLNWDAFPKLGKGLRSATPDAQ

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FIGURE 130

CAGTTCTGAAATCAATGGAGTTAATTTAGGGAATACAAACCAGCCATGGGGGTGGAGATTGC
CTTTGCCTCAGTGATTCTCACCTGCCTCTCCCTTCTGGCAGCAGGAGTCTCCCAGGTTGTTC
TTCTCCAGCCAGTTCCAACCTCAGGAGACAGGTCCCAAGGCCATGGGAGATCTCTCCTGTGGC
TTTGCCGGCCACTCATGAGAGAGTGTTTTTGTGTAAAGTATTTTTTAGAATACTGTTGACTTCT
TCATGATTTAATAACCATCCTTTGCGAAGTTTTATGAGGCTTTAGGGGAATGTCAACCCCTCA
AATTTTTGTTATACTAGATGGCTTCCATTTACCCACCACTATTTTAAGGTCCCTTTATTTTT
AGGTTCAAGGTTCAATTTGACTTGAGAAAGTGCCCTTCTGCAGCTTCATTGATTTTGTATTATC
TTCATTAATTGTAACGATTAAAAAAGAATAAGAGCACGCAGACCTCTAGGAGAATATTT
TATCCCTGGGTGCCCCTGACACATTTATGTAGTGATCCCACAAATGTGATTGTTAATTTAAA
TGTTATTCTAATATTAGTACATTCAGTTGTGATGTAATATGAATAACCAGAATCTATTTCTT
AAAAGTTTTGAGTATATTTTTCAACTAGATATTTGTATAGAAAGACTGAATAGTGATG

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FIGURE 131

MGVEIAFASVILTCLSLAAGVSQVLLQPVPTQETGPKAMGDLSCGFAGHS

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FIGURE 132

GGGGAATCTGCAGTAGGTCTGCCGGCGATGGAGTGGTGGGCTAGCTCGCCGCTTCGGCTCTG
GCTGCTGTTGTTCCCTCCTGCCCTCAGCGCAGGGCCGCCAGAAGGAGTCAGGTTCAAAATGGA
AAGTATTTATTGACCAAATTAACAGGTCTTTGGAGAATTACGAACCATGTTCAAGTCAAAAC
TGCAGCTGCTACCATGGTGTCTAGAGAAGAGGATCTAACTCCTTTCCGAGGAGGCATCTCCAG
GAAGATGATGGCAGAGGTAGTCAGACGGAAGCTAGGGACCCACTATCAGATCACTAAGAACA
GACTGTACCCGGGAAAATGACTGCATGTTCCCTCAAGGTGTAGTGGTGTGAGCACTTTATT
TTGGAAGTGATCGGGCGTCTCCCTGACATGGAGATGGTGATCAATGTACGAGATTATCCTCA
GGTTCCTAAATGGATGGAGCCTGCCATCCCAGTCTTCTCCTTCAGTAAGACATCAGAGTACC
ATGATATCATGTATCCTGCTTGGACATTTTGGGAAGGGGGACCTGCTGTTTGGCCAATTTAT
CCTACAGGTCTTGGACGGTGGGACCTCTTCAGAGAAGATCTGGTAAGGTCAGCAGCACAGTG
GCCATGGAAAAAGAAAACTCTACAGCATATTTCCGAGGATCAAGGACAAGTCCAGAACGAG
ATCCTCTCATTTCTTCTGTCTCGGAAAAACCCAAAACCTGTTGATGCAGAATACACCAAAAAC
CAGGCCCTGGAAATCTATGAAAGATACCTTAGGAAAGCCAGCTGCTAAGGATGTCCATCTTGT
GGATCACTGCAAATACAAGTATCTGTTTAATTTTCGAGGCGTAGCTGCAAGTTTCCGGTTTA
AACACCTCTTCCTGTGTGGCTCACTTGTTTTCCATGTTGGTGATGAGTGGCTAGAATTCTTC
TATCCACAGCTGAAGCCATGGGTCACTATATCCCAGTCAAAACAGATCTCTCCAATGTCCA
AGAGCTGTTACAATTTGTAAAAGCAAATGATGATGTAGCTCAAGAGATTGCTGAAAGGGGAA
GCCAGTTTATTAGGAACCATTTGCAGATGGATGACATCACCTGTTACTGGGAGAACCTCTTG
AGTGAATACTCTAAATTCCTGTCTTATAATGTAACGAGAAGGAAAGGTTATGATCAAATTAT
TCCCAAAATGTTGAAAACGAACTATAGTAGTCATCATAGGACCATAGTCCTCTTTGTGGCA
ACAGATCTCAGATATCCTACGGTGAGAAGCTTACCATAAGCTTGGCTCCTATACCTTGAATA
TCTGCTATCAAGCCAAATACCTGGTTTTCTTATCATGCTGCACCCAGAGCAACTCTTGAGA
AAGATTTAAAATGTGTCTAATACACTGATATGAAGCAGTTCAACTTTTGGATGAATAAGGA
CCAGAAATCGTGAGATGTGGATTTTGAACCCAACTCTACCTTTCATTTCTTAAGACCAATC
ACAGCTTGTGCCTCAGATCATCCACCTGTGTGAGTCCATCACTGTGAAATTGACTGTGTCCA
TGTGATGATGCCCTTTGTCCCATTATTTGGAGCAGAAAATTCGTCAATTTGGAAGTAGTACAA
CTCATTTGCTGGAATTGTGAAATTATTCAGGCGTGATCTCTGTCACTTTATTTTAATGTAGG
AAACCTTATGGGGTTTATGAAAAATACTTGGGGATCATTCTCTGAATGGTCTAAGGAAGCGG
TAGCCATGCCATGCAATGATGTAGGAGTTCTCTTTTGTAAAACCATAAACTCTGTTACTCAG
GAGGTTTCTATAATGCCACATAGAAAGAGGCCAATTGCATGAGTAATTATTGCAATTGGATT
TCAGGTTCCCTTTTTGTGCCTTCATGCCCTACTTCTTAATGCCTCTCTAAAGCCAAA

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FIGURE 133

MEWWASSPLRLWLLLFLPSAQGRQKESGSKWKVFIHQINRSLENYEPCSSQNCSCYHGVIE
EDLTPFRGGISRKMAEVVRRKLGTHYQITKNRLYREND CMFPSRCSGVEHFILEVIGRLPD
MEMVINVRDYPQVPKWMEPAIPVFSFSKTSEYHDI MPAWTFWEGGPAVWPIYPTGLGRWDL
FREDLVRSAQWPWKKNSTAYFRGSRTSPERDPLILLSRKNPKLVDAEYTKNQAWKSMKDT
LGKPAAKDVHLVDHCKYKYLNFNFRGVAASFRFKHLFLCGSLVFHVGD EWLEFFYPQLKPWVH
YIPVKTDLSNVQELLQFVKANDDVAQEIAERGSQFIRNHLQMDDITCYWENLLSEYSKFLSY
NVTRRKGYDQIIPKMLKTEL

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FIGURE 134

CACCCCTCCATTTCTCGCCATGCCCCCTGCACTGCTCCTGATCCCTGCTGCCCTCGCCTCTT
TCATCCTGGCCTTTGGCACCGGAGTGGAGTTCGTGCGCTTACCTCCCTTCGGCCACTTCTT
GGAGGGATCCCGGAGTCTGGTGGTCCGGATGCCCGCCAGGGATGGCTGGCTGCCCTGCAGGA
CCGCAGCATCCTTGCCCCCTGGCATGGGATCTGGGGCTCCTGCTTCTATTTGTTGGGCAGC
ACAGCCTCATGGCAGCTGAAAGAGTGAAGGCATGGACATCCCGGTACTTTGGGGTCTTCAG
AGGTCACTGTATGTGGCCTGCACTGCCCTGGCCTTGACAGCTGGTGATGCGGTACTGGGAGCC
CATACCCAAAGGCCCTGTGTTGTGGGAGGCTCGGGCTGAGCCATGGGCCACCTGGGTGCCGC
TCCTCTGCTTTGTGCTCCATGTATCTCCTGGCTCCTCATCTTTAGCATCCTTCTCGTCTTT
GACTATGCTGAGCTCATGGGCCTCAAACAGGTATACTACCATGTGCTGGGGCTGGGCGAGCC
TCTGGCCCTGAAGTCTCCCGGGCTCTCAGACTCTTCTCCACCTGCGCCACCCAGTGTGTG
TGGAGCTGCTGACAGTGCTGTGGGTGGTGCCTACCCTGGGCACGGACCGTCTCCTCCTTGCT
TTCTCCTTACCCTCTACCTGGGCCTGGCTCACGGGCTTGATCAGCAAGACCTCCGCTACCT
CCGGGCCCAGCTACAAAGAAACTCCACCTGCTCTCTCGGCCCCAGGATGGGGAGGCAGAGT
GAGGAGCTCACTCTGGTTACAAGCCCTGTTCTTCTCTCCCACTGAATTCTAAATCCTTAAC
ATCCAGGCCCTGGCTGCTTCATGCCAGAGGCCCAAATCCATGGACTGAAGGAGATGCCCCCTT
CTACTACTTGAGACTTTATTCTCTGGGTCCAGCTCCATACCCTAAATTCTGAGTTTCAGCCA
CTGAACTCCAAGGTCCACTTCTCACCAGCAAGGAAGAGTGGGGTATGGAAGTCATCTGTCCC
TTCACTGTTTAGAGCATGACACTCTCCCCCTCAACAGCCTCCTGAGAAGGAAAGGATCTGCC
CTGACCACTCCCCCTGGCACTGTTACTTGCCTCTGCGCCTCAGGGGTCCCCCTTCTGCACCGCT
GGCTTCCACTCCAAGAAGGTGGACCAGGGTCTGCAAGTTCAACGGTCATAGCTGTCCCTCCA
GGCCCCAACCTTGCCTCACCCTCCCGGCCCTAGTCTCTGCACCTCCTTAGGCCCTGCCTCT
GGGCTCAGACCCCAACCTAGTCAAGGGGATTCTCCTGCTCTTAACTCGATGACTTGGGGCTC
CCTGCTCTCCCGAGGAAGATGCTCTGCAGGAAAATAAAAGTCAGCCTTTTTCTAAAAAAA

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FIGURE 135

MAPALLLIPAA LASFILAFGTGVEFVRFTSLRPLLGGIPESGGPDARQGWL AALQDRSILAP
LAWDLGLLLLFVGQHS LMAAERVKAWTSRYFGVLQRS LYVACTALALQLVMRYWEP I PKGPV
LWEARAEPWATWVPLLCFVLHVISWLLIFSI LLVFDYAELMGLKQVYYHVLGLGEPLALKSP
RALRLFSHLRHPVCVELLTVLWVPTLGTDRLLLAFLLTLYLGLAHGLDQQDLRYLRAQLQR
KLHLLSRPQDGEAE

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FIGURE 136

CCGAGCACAGGAGATTGCCTGCGTTTAGGAGGTGGCTGCGTTGTGGGAAAAGCTATCAAGGA
AGAAATTGCCAAACCATGTCTTTTTTCTGTTTT CAGAGTAGTTCAACAACAGATCTGAGTGT
TTTAATTAAGCATGGAATACAGAAAAACAACAAAAA CTTAAGCTTTAATTT CATCTGGAATT
CCACAGTTTTCTTAGCTCCCTGGACCCGGTTGACCTGTTGGCTCTTCCCGCTGGCTGCTCTA
TCACGTGGTGCTCTCCGACTACTCACCCGAGTGTAAGAACCTTCGGCTCGCGTGCTTCTG
AGCTGCTGTGGATGGCCTCGGCTCTCTGGACTGTCTTCCGAGTAGGATGTCAC TGAGATCC
CTCAAATGGAGCCTCCTGCTGCTGTCACTCCTGAGTTTCTTTGTGATGTGGTACCTCAGCCT
TCCCCACTACAATGTGATAGAACGCGTGAAC TGGATGTACTTCTATGAGTATGAGCCGATT
ACAGACAAGACTTTCACTTCACACTTCGAGAGCATTCAA CTGCTCTCATCAAAATCCATT
CTGGTCATTCTGGTGACCTCCACCCCTTCAGATGTGAAAGCCAGGCAGGCCATTAGAGTTAC
TTGGGGTGAAAAAAGTCTTGGTGGGGATATGAGGTTCTTACATTTTTCTTATTAGGCCAAG
AGGCTGAAAAGGAAGACAAAATGTTGGCATTGTCTT TAGAGGATGAACACCTTCTTTATGGT
GACATAATCCGACAAGATTTTTTAGACACATATAATAACCTGACCTTGAAAACCATTTATGGC
ATT CAGGTGGGTAAC TGAGTTTTGCCCAATGCCAAGTACGTAATGAAGACAGACACTGATG
TTTTCATCAATACTGGCAATTTAGTGAAGTATCTTTTAAACCTAAACCACTCAGAGAAGTTT
TTCACAGGTTATCCTCTAATTGATAATTATTCCTATAGAGGATTTTACCAAAAAACCCATAT
TTCTTACCAGGAGTATCCTTTCAAGGTGTTCCCTCCATACTGCAGTGGGTGGGTATATAA
TGTC CAGAGATTTGGTGCCAAGGATCTATGAAATGATGGGT CACGTAAAACCCATCAAGTTT
GAAGATGTTTATGTGCGGATCTGTTTGAATTTATTAAAAGTGAACATT CATATTCAGAAGA
CACAAATCTTTTCTTTCTATATAGAATCCATT TGGATGTCTGTCAACTGAGACGTGTGATTG
CAGCCCATGGCTTTTCTTCCAAGGAGATCATCACTTTT TGGCAGGTCATGCTAAGGAACACC
ACATGCCATTATTAACCTTCACATTCTACAAAAAGCCTAG AAGGACAGGATACCTTGTGGAAA
GTGTTAAATAAAGTAGGTACTGTGGAAAATTCATGGGGAGGTCAGTGTGCTGGCTTACACTG
AACTGAAACTCATGAAAAACCCAGACTGGAGACTGGAGGGTTACACTTGTGATTTATTAGTC
AGGCCCTTCAAAGATGATATGTGGAGGAATTAAATATAAAGGAATTGGAGGTTTTTGTCTAAA
GAAATTAATAGGACCAAACAATTTGGACATGTCACTTCTGTAGACTAGAAATTTCTTAAAAGGG
TGTTACTGAGTTATAAGCTCACTAGGCTGTAAAAACAAAACAATGTAGAGTTTTTATTATTG
AACAAATGTAGTCACTTGAAGGTTTTTGTGTATATCTTATGTGGATTACCAATTTAAAAATATA
TG TAGTTCTGTGTCAAAAAACTTCTTCACTGAAGTTATACTGAACAAAATTTTACCTGTTTT
TGGTCATTTTATAAAGTACTTCAAGATGTTGCAGTATTT CACAGTTATTATTATTTAAAATTA
CTTCAACTTTTGTGTTTTTAAATGTTTTGACGATTTCAATACAAGATAAAAAAGGATAGTGAAT
CATTCTTTACATGCAAACATTTTCCAGTTACTTAACTGATCAGTTTATTATTGATACATCAC
TCCATTAATGTAAAGTCATAGGTCATTATTGCATATCAGTAATCTCTTGGACTTTGTTAAAT
ATTTTACTGTGGTAATATAGAGAAGAATTAAAGCAAGAAAATCTGAAAA

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FIGURE 137

MASALWTVLP SRMSLRSLKWSLLLLSLLSFFVMWYLSLPHYNVIERVNW MYFYEYEP IYRQD
FHFTLR:EH SNCSHQ NPFLVILVTSH PSDVKARQAIRVTWGEKKS WWGYEVLTFLLGQEA EK
EDKMLALSLEDEHLLYGD IIRQDFLD TYNNLT LKTIMAFRWVTEFCPNAKYVMKTD TDVF IN
TGNLVKYLLNLNHSEKFFTGYPLIDNYSYRGFYQKTHISYQEYPFKVFPPYCSGLGYIMSRD
LVPRIYEMMGHV KPIKFEDVYVGICLNLLKVNIHIPEDTNLFFLYRIHLDVCQLRRVIAAHG
FSSKEIITFWQVMLRNTTCHY

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FIGURE 138

CCTCTGTCCACTGCTTTCGTGAAGACAAGATGAAGTTCACAATTGTCTTTGCTGGACTTCTT
GGAGTCTTTCTAGCTCCTGCCCTAGCTAACTATAATATCAACGTCAATGATGACAACAACAA
TGCTGGAAGTGGGCAGCAGTCAGTGAGTGTCAACAATGAACACAATGTGGCCAATGTTGACA
ATAACAACGGATGGGACTCCTGGAATTCCATCTGGGATTATGGAAATGGCTTTGCTGCAACC
AGACTCTTTCAAAAGAAGACATGCATTGTGCACAAAATGAACAAGGAAGTCATGCCCTCCAT
TCAATCCCTTGATGCACTGGTCAAGGAAAAGAAGCTTCAGGGTAAGGGACCAGGAGGACCAC
CTCCCAAGGGCCTGATGTACTCAGTCAACCCAAACAAAGTCGATGACCTGAGCAAGTTCGGA
AAAAACATTGCAAACATGTGTCTGTGGGATTCCAACATACATGGCTGAGGAGATGCAAGAGGC
AAGCCTGTTTTTTTACTCAGGAACGTGCTACACGACCAGTGTACTATGGATTGTGGACATTT
CCTTCTGTGGAGACACGGTGGAGAACTAAACAATTTTTTAAAGCCACTATGGATTTAGTCAT
CTGAATATGCTGTGCAGAAAAAATATGGGCTCCAGTGGTTTTTACCATGTCATTCTGAAATT
TTTCTCTACTAGTTATGTTGATTTCTTTAAGTTTCAATAAAATCATTTAGCATTGAAAAAAA

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FIGURE 139

MKFTIVFAGLLGVFLAPALANYNINVNDDNNNAGSGQSVSVNNEHNVANVDNNGWDSWNS
IWDYGNGFAATRLFQKKTCIVHKMNKEVMPSIQSLDALVKEKKLQGKGPGGPPPKGLMYSVN
PNKVDDLKFGKNIANMCRGIPTYMAEEMQEASLFFYSGTCYTTSVLWIVDISFCGDTVEN

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FIGURE 140

CATTTCTGAAACTAATCGTGTGAGAATTGACTTTGAAAAGCATTGCTTTTTACAGAAGTATA
TTAACTTTTTAGGAGTAATTTCTAGTTTGGATTGTAATATGAAATAATTTAAAAGGGCTTCG
CTCATATATAGGAAAATCGCATATGGTCCTAGTATTAAATCTTATTGCTTACTGATTTTTT
TGAGTTAAGAGTTGTTATATGCTAGAAATATGAGGATGTGAATATAAATAAGAGAAGAAAAA
GAATAAAGTAGATTGAGTCTCCAATTTTATGTAAGCTTCAGAAGAACTGGTTTGTGTACATG
CAAGCTTATAGTTGAAATATTTTTTCAGGAATTACATGAATGACAGTCTTCGAACCAATGTGT
TTGTTTCGATTTCAACCAGAGACTATAGCATGTGCTTGCATCTACCTTGCAGCTAGAGCACTT
CAGATTCGGTTGCCAACTCGTCCCCATTGGTTTTCTTCTTTTTGGTACTACAGAAGAGGAAAT
CCAGGAAATCTGCATAGAAACACTTAGGCTTTATACCAGAAAAAGCCAACTATGAATTAC
TGGAAAAAGAAGTAGAAAAAAGAAAAAGTAGCCTTACAAGAAGCCAAATTTAAAGCAAAGGGA
TTGAATCCGGATGGAACCTCAGCCCTTTCAACCCTGGGTGGATTTTCTCCAGCCTCCAAGCC
ATCATCACCAGAGAAGTAAAAGCTGAAGAGAAATCACCAATCTCCATTAATGTGAAGACAG
TCAAAAAAGAACCTGAGGATAGACAACAGGCTTCCAAAAGCCCTTACAATGGTGTAAGAAAA
GACAGCAAGAGAAGTAGAAATAGCAGAAGTGCAAGTCGATCGAGGTCAAGAACACGATCAGG
TTCTAGATCACATACTCCAAGAAGACACTATAATAATAGGCGGAGTCGATCTGGAACATACA
GCTCGAGATCAAGAAGCAGGTCCCGCAGTCACAGTGAAAGCCCTCGAAGACATCATAATCAT
GGTTCCTCCTCACCTTAAGGCCAAGCATAACAGAGATGATTTAAAAAGTTCAAACAGACATGG
TCATAAAAGGAAAAAATCTCGTTCTCGATCTCAGAGCAAGTCTCGGGATCACTCAGATGCAG
CCAAGAAACACAGGCATGAAAGGGGACATCATAGGGACAGGCGTGAACGATCTCGCTCCTTT
GAGAGGTCCCATAAAAGCAAGCACCATGGTGGCAGTCGCTCAGGACATGGCAGGCACAGGCG
CTGA~~CT~~CTTTCTCTTCCTTTGAGCCTGCATCAGTTCTTGGTTTTGCCTATCTACAGTGTGATGT
ATGGACTCAATCAAAAACATTAAACGCAAACCTGATTAGGATTTGATTTCTTGAAACCCCTCTA
GGTCTCTAGAACACTGAGGACAGTTTCTTTTGAAAAGAACTATGTTAATTTTTTTGCACATT
AAAATGCCCTAGCAGTATCTAATTAAAAACCATGGTCAGGTTCAATTGTACTTTATTATAGT
TGTGTATTGTTTATTGCTATAAGAACTGGAGCGTGAATTCTGTAAAAATGTATCTTATTTTT
ATACAGATAAAATTGCAGACACTGTTCTATTTAAGTGGTTATTTGTTTAAATGATGGTGAAT
ACTTTCTTAACACTGGTTTGTCTGCATGTGTAAAGATTTTACAAGGAAATAAAATACAAAT
CTTGTTTTTTCTAAAAAAGAAAAAAGT

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FIGURE 141

MNDSLRTNVFVRFQPETIACACIYLAARALQIPLPTRPHWFLFLFGTTEEEIQEICIETLRLY
TRKKPNYELLEKEVEKRRKVALQEAKLKAKGLNPDGTPALSTLGGFSFASKPSSPREVKAEEK
SPISINVKTVKKEPEDRQQASKSPYNGVRKDSKRSRNSRSASRSRSRTRSRSRSHTPRRHYN
NRRSRSGTYSSRSRSHSESPRRHHNHGSPHLKAKHTRDDLKSSNRHGHRKRSRSQ
SKSRDHSDAAKKHRHERGHRDRRERSRSFERSHKSKHHGGSRSRSGHGRHR

FIGURE 142

TGGGGATAAAGGAAAAATGGTCAGGTATTAATGGCTTAAAGATTATTGGAAGGGGTTTATCA
TTTTTTGAANNTATTTCGGGTCANAATTGNCTTTGAAAAGCATTGCTTTTTACAGAAATATAT
TANCTTTTTAGAGTAATTTCTAGTTTGGATTGTAATATGAAATTATTTAAAAGGGCTTCGCT
CATATATAGGAAAATCGCATATGGTCCTAGTATTAAATTNTTATTGCTTACTGATTTTTTTG
AGTTAAGAGTTGTTATATGNTAGAATATGAGGATGTGAATATAAATAAGAGAAGAAAAAAGA
ATAAAGTAGATTGAGTCTCCAATTTTATGTAAGCTTCAGAAGAAGCTGGTTTGTTTACATGCA
AGCTTATAGTTGAAATATTTTTCAGGAATTACATGAATGACAGTCTTCGAACCAATGTGTTT
GTTTCGATTTCAACCAGAGANTATAGCATGTGCTTGCATCTACCTTGCAGNTAGAGCACTTCA
GATTCCGTTGCCAACTNGTCCCCATTGGTTTCTTCTTTTGGTACTACAGAAGAGGAAATCC
AGGAAATNTGCATAGAAACACTTAGGCTTTATACCAGAAAAAAGCCAAACTATGAATTACTG
GAAAAAGAAGTAGAAAAAAGAAAAGTAGCCTTACAAGAAGCCNAATTAAAAGCAAAGGGATT
GAATCCGGATGGAACTCCAGCCCTTTCAACCCTGGGTGGATTTTCTCC

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FIGURE 143

GGCACGAGGCCTCGTGCCAAGCTTGGCACGAGGGTGACCGCGTTCTCGCACGCGTCAATGGC
GGTCCTCGGAGTACAGCTGGTGGTGACCCTGCTCACTGCCACCCTCATGCACAGGCTGGCGC
CACACTGCTCCTTCGCGCGCTGGCTGCTCTGTAACGGCAGTTTGTTCGGATACAAGCACCCG
TCTGAGGAGGAGCTTCGGGCCCTGGCGGGGAAGCCGAGGCCAGAGGCAGGAAAGAGCGGTG
GGCCAATGGCCTTAGTGAGGAGAAGCCACTGTCTGTGCCCCGAGATGCCCCGTTCCAGCTGG
AGACCTGCCCCCTCACGACCGTGATGCCCTGGTCTGCGCTTCTTCCTGGAGTACCAGTGG
TTTGTGGACTTTGCTGTGTACTCGGGCGGCGTGACCTCTTCACAGAGGCCTACTACTACAT
GCTGGGACCAGCCAAGGAGACTAACATTGCTGTGTTCTGGTGCCCTGCTCACGGTGACCTTCT
CCATCAAGATGTTCCCTGACAGTGACACGGCTGTACTTCAGCGCCGAGGAGGGGGGTGAGCGC
TCTGTCTGCCCTCACCTTTGCCCTTCCTCTTCCTGCTGCTGGCCATGCTGGTGCAAGTGGTGCG
GGAGGAGACCCTCGAGCTGGGCCTGGAGCCTGGTCTGGCCAGCATGACCCAGAACTTAGAGC
CACTTCTGAAGAAGCAGGGCTGGGACTGGGCGCTTCCTGTGGCCAAGCTGGCTATCCGCGTG
GGACTGGCAGTGGTGGGCTCTGTGCTGGGTGCCTTCCTCACCTTCCCAGGCCTGCGGCTGGC
CCAGACCCACCGGGACGCACTGACCATGTGCGAGGACAGACCCATGCTGCAGTTCCTCCTGC
ACACCAGCTTCCTGTCTCCCCTGTTTCATCCTGTGGCTCTGGACAAAGCCCATTGCACGGGAC
TTCCTGCACCAGCCGCGTTTGGGGAGACGCGTTTCTCCCTGCTGTCCGATTCTGCCTTCGA
CTCTGGGCGCCTCTGGTTGCTGGTGGTGCTGTGCCTGCTGCGGCTGGCGGTGACCCGGCCCC
ACCTGCAGGCCTACCTGTGCCTGGCCAAGGCCCGGGTGGAGCAGCTGCGAAGGGAGGCTGGC
CGCATCGAAGCCCGTGAAATCCAGCAGAGGGTGGTCCGAGTCTACTGCTATGTGACCGTGGT
GAGCTTGCAGTACCTGACGCCGCTCATCCTCACCCCTCAACTGCACACTTCTGCTCAAGACGC
TGGGAGGCTATTCTGGGGCCTGGGCCCAGCTCCTCTACTATCCCCCGACCCATCCTCAGCC
AGCGCTGCCCCCATCGGCTCTGGGGAGGACGAAGTCCAGCAGACTGCAGCGCGGATTGCCGG
GGCCCTGGGTGGCCTGCTTACTCCCCCTCTTCCTCCGTGGCGTCTGGCCTACCTCATCTGGT
GGACGGCTGCCTGCCAGCTGCTCGCCAGCCTTTTCGGCCTCTACTTCCACCAGCACTTGGCA
GGCTCCTAGCTGCCTGCAGACCCTCCTGGGGCCCTGAGGTCTGTTCTGGGGCAGCGGGACA
CTAGCCTGCCCCCTCTGTTTGGCCCCCGTGTCCCCAGCTGCAAGGTGGGGCCGGACTCCCC
GGCGTTCCCTTCACCACAGTGCTGACCCGCGGCCCCCCTTGGACGCCGAGTTTCTGCCTCA
GAACTGTCTCTCCTGGGCCCAGCAGCATGAGGGTCCCGAGGCCATTGTCTCCGAAGCGTATG
TGCCAGGTTTGAGTGGCGAGGGTGATGCTGGCTGCTCTTCTGAACAAATAAAGGAGCATGCC
GATTTTAA

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FIGURE 144

MAVLGVQLVVTLLTATLMHRLAPHCSFARWLLCNGSLFRYKHPSEEELRALAGKPRPRGRKE
RWANGLSEEKPLSVPRDAPFQLETCPLTTVDALVLRFFLEYQWFVDFAVYSGGVYLFTEAYY
YMLGPAKETNIAVFWCLLTVTFSIKMFLT VTRLYFSAEEGGERSVCLTFAFLFLLLAMLVQV
VREETLELGLPGLASMTQNLEPLLKKQGWDWALPVAKLAI RVGLAVVGSVLGAFLTFPGLR
LAQTHRDALTMSEDRPMLQFLLHTSFLSPLFILWLWTKPIARDFLHQPPFGETRFSLLSDSA
FDSGRLWLLVVLCLLR LAVTRPHLQAYLCLAKARVEQLRREAGRIEAREIQQRVVRVYCYVT
VVS LQYLTP LILTLNCTLLKTLGGYSWGLGPAPLLSPDPSSASAAPIGSGEDEVQQTAA RI
AGALGGLLTPLFLRGVLAYLIWWT AACQLLASLFGLYFHQHLA GS

FIGURE 145

CGTTNGCACGCGTCAATGGCGGTCTCGGAGTACAGCTGGTGGTGACCCTGCTCACTGCCAC
CCTCATGCACAGGCTGGCGCCACACTGCTCCTTCGCGCGCTGGCTGCTCTGTAACGGCAGTT
TGTTCGGATACAAGCACCCGTNTTGAGGAGGAGCTTCGGGGCCCTGGCGGGGAAGCCGAGGCC
CAGAGGCAGGAAAGAGCGGTGGGCCAATGGCCTTAGTGAGGAGAAGCCACTGTCTGTGCCCC
GAGATGCCCCGTTCCAGCTGGAGACCTGCCCCCTCACGACCGTGGATGCCCTGGTCCTGCGC
TTCTTCCTGGAGTACCAGTGGTTTGTGGACTTTGCTGTGTACTCGGGCGGCGTGACCTCTT
CACAGAGGCCTACTACTACATGCTGGGACCAGCCAAGGAGACTAACATTGCTGTGTTCTGGT
GCCTGCTCACAGTGACCTTCTCCATCAAGATGTTCTGACAGTGACACGGCTGTACTTCAGC
GCCGAGGAGGGGGGTGAGCGCTCTGTCTGCCTCACCTTTGCCTTCCTCTTCCTGCTGCTGGC
CATGCTGGTGCAAGCG

FIGURE 146

GGTTCCTACATCCTCTCATCTGAGAATCAGAGAGCATAATCTTCTTACGGGGCCCGTGATTTA
TTAACGTGGCTTAATCTGAAGGTTCTCAGTCAAATCTTTGTGATCTACTGATTGTGGGGGC
ATGGCAAGGTTTGGCTTAAAGGAGCTTGGCTGGTTTGGGGCCCTTGTTAGCTGACAGAAGGTGGC
CAGGGAGAATGCAGCACACTGCTCGGAGAAATGAAGGCGCTTCTGTTGCTGGTCTTGCCCTTGG
CTCAGTCCTGCTAACTACATTGACAAATGTGGGCAACCTGCACTTCCTGTATTGAGAACTCTG
TAAAGGTGCCCTCCCCTACGGCCTGACCAAAGATAGGAAGAGGCGCTCACAAGATGGCTGTC
CAGACGGCTGTGCGAGCCTCACAGCCACGGCTCCCCTCCCAGAGGTTTCTGCAGCTGCCACC
ATCTCCTTAATGACAGACGAGCCTGGCCTAGACAACCCTGCCCTACGTGTCTCGGCAGAGGA
CGGGCAGCCAGCAATCAGCCCAGTGGACTCTGGCCGGAGCAACCGAACTAGGGCACGGCCCT
TTGAGAGATCCACTATTAGAAGCAGATCATTTAAAAAATAAATCGAGCTTTGAGTGTCTTT
CGAAGGACAAAGAGCGGGAGTGCAGTTGCCAACCATGCCGACCAGGGCAGGGAAAATTCTGA
AAACACCCTGCCCCCTGAAGTCTTTCCAAGGTTGTACCACCTGATTCCAGATGGTGAAATTA
CCAGCATCAAGATCAATCGAGTAGATCCCAGTGAAAGCCTCTCTATTAGGCTGGTGGGAGGT
AGCGAAACCCCACTGGTCCATATCATTATCCAACACATTTATCGTGATGGGGTGATCGCCAG
AGACGGCCGGCTACTGCCAGGAGACATCATTCTAAAGGTCAACGGGATGGACATCAGCAATG
TCCCTCACAACCTACGCTGTGCGTCTCCTGCGGCAGCCCTGCCAGGTGCTGTGGCTGACTGTG
ATGCGTGAAACAGAAGTTCCGCAGCAGGAACAATGGACAGGCCCCGGATGCCCTACAGACCCCG
AGATGACAGCTTTTCTGTGATTCTCAACAAAAGTAGCCCCGAGGAGCAGCTTGGAAATAAAAC
TGGTGCAGCAAGGTGGATGAGCCTGGGGTTTTTCATCTTCAATGTGCTGGATGGCGGTGTGGCA
TATCGACATGGTCAGCTTGAGGAGAATGACCGTGTGTTAGCCATCAATGGACATGATCTTCG
ATATGGCAGCCCAGAAAGTTCGGGCTCATCTGATTTCAGGCCAGTGAAAGACGTGTTACCTCG
TCGTGTCCCCGCCAGGTTCCGGCAGCGGAGCCCTGACATCTTTTCAGGAAGCCGGCTGGAACAGC
AATGGCAGCTGGTCCCCAGGGCCAGGGGAGAGGAGCAACACTCCCAAGCCCCCTCCATCCTAC
AATTACTTGTCTATGAGAAGGTGGTAAATATCCAAAAGACCCCGGTGAATCTCTCGGCATGA
CCGTGCGAGGGGGAGCATCACATAGAGAATGGGATTTGCCTATCTATGTCATCAGTGTGAG
CCCGGAGGAGTCATAAGCAGAGATGGAAGAATAAAAAAGGTGACATTTTGTGTAATGTGGA
TGGGGTCGAACTGACAGAGGTGAGCCGGAGTGAGGCAGTGGCATTATTGAAAAGAACATCAT
CCTCGATAGTACTCAAAGCTTTGGAAGTCAAAGAGTATGAGCCCCAGGAAGACTGCAGCAGC
CCAGCAGCCCTGGACTCCAACCACAACATGGCCCCACCCAGTGACTGGTCCCCATCCTGGGT
CATGTGGCTGGAATTACCACGGTGCTTGTATACTGTAAAGATATTGTATTACGAAGAAACA
CAGCTGGAAGTCTGGGCTTCTGCATTGTAGGAGGTTATGAAGAATACAATGGAAACAAACCT
TTTTTTCATCAAATCCATTGTTGAAGGAACACCAGCATACAATGATGGAAGAATTAGATGTGG
TGATATTCTTCTGTGTCAATGGTAGAAGTACATCAGGAATGATACATGCTTGCTTGGCAA
GACTGCTGAAAGAACTTAAAGGAAGAATTACTCTAACTATTGTTTCTTGGCCTGGCAGTTTTT
TTATAAATCAATGATGGGTGAGGAAAACAGAAAAATCACAAATAGGCTAAGAAGTTGAA
ACACTATATTTATCTTGTGAGTTTTTATATTTAAAGAAAGAAATACATTGTAAAAATGTCAGG
AAAAGTATGATCATCTAATGAAAGCCAGTTACACCTCAGAAAAATATGATTCCAAAAAATTA
AACTACTAGTTTTTTTTTTCAGTGTGGAGGATTTCTCATTACTCTACAACATTGTTTATATTT
TTTCTATTCAATAAAAAGCCCTAAAACAATAAAATGATTGATTGTATACCCCACTGAATT
CAAGCTGATTTAAATTTAAATTTGGTATATGCTGAAGTCTGCCAAGGGTACATTATGGCCA
TTTTTAATTTACAGCTAAAATATTTTTTAAATGCATTGCTGAGAAACGTTGCTTTTCATCAA
ACAAGAATAAATATTTTTTCAGAAGTTAAA

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FIGURE 147

MKALLLLVLPWLSPANYIDNVGNLHFLYSELCKGASHYGLTKDRKRRSQDGCPCDGCASLTAT
APSPEVSAAATISLMTDEPGLDNPAYVSSAEDGQPAISPVDSGRSNRTRARPFERSTIRSRS
FKKINRALSVLRRTKSGSAVANHADQGRESENTTAPEVFPRLYHLIPDGEITSIKINRVDP
SESLSIRLVGGSETPLVHII IQHIYRDGVIARDGRLLPGDIILKVNGMDISNVPHNYAVRLL
RQPCQVLWLTVMREQKFRSRNNGQAPDAYRPRDDSFHVILNKSSPEEQLGIKLVRKVDEPGV
FIFNVLDGGVAYRHGQLEENDRVLAINGHDLRYGSPESA AHLI QASERRVHLVVSQRQVRQRS
PDIFQEAGWNSNGSWSPGPGERSNTPKPLHPTITCHEKVVNIQKDPGESLGMTVAGGASHRE
WDLPIYVISVEPGGVISRDGRIKTDILLNVDGVELTEVSRSEAVALLKRTSSSIVLKALEV
KEYEPQEDCSSPAALDSNHNMAPPSDWSPSWVMWLELPRCLYNCKDIVLRRNTAGSLGFCIV
GGYEEYNGNKPFPIKSIVEGTPAYNDGRIRCGDILLAVNGRSTSGMIHACLARLLKELKGRI
TLTIVSWPGTFL

FIGURE 148

CCAAAGTGATCATTTGAAAAAGAGATATCCACATCTTCAAGCCCATATAAAGGATAGAAGCT
GCACAGGGCAGCTTTACTTACTCCAGCACCTTCCTCTCCCAGGCAAATGGTGCTGACCATCT
TTGGGATACAATCTCATGGATACGAGGTTTTTAACATCATCAGCCCAAGCAACAATGGTGGC
AATG TTCAGGAGACAGTGACAATTGATAATGAAAAAATACCGCCATCGTTAACATCCATGC
AGGATCATGCTCTTCTACCACAATTTTTGACTATAAACATGGCTACATTGCATCCAGGGTGC
TCTCCCGAAGAGCCTGCTTTATCCTGAAGATGGACCATCAGAACATCCCTCCTCTGAACAAT
CTCCAATGGTACATCTATGAGAAACAGGCTCTGGACAACATGTTCTCCAACAAATACACCTG
GGTCAAGTACAACCCTCTGGAGTCTCTGATCAAAGACGTGGATTGGTTCCTGCTTGGGTCAC
CCATTGAGAACTCTGCAAACATATCCCTTTGTATAAGGGGGAAGTGGTTGAAAACACACAT
AATGTCGGTGCTGGAGGCTGTGCAAAGGCTGGGCTCCTGGGCATCTTGGGAATTTCAATCTG
TGCAGACATTATGTTTAGGATGATTAGCCCTCTTGTTTTATCTTTTCAAAGAAATACATCC
TTGGTTTACACTCAAAGTCAAATTAAATTCTTTCCCAATGCCCCAACTAATTTTGAGATTC
AGTCAGAAAATATAAATGCTGTATTTATA

FIGURE 149

MKILVAFLVVLTFGIQSHGYEVFNIIISPSNNGGNVQETVTIDNEKNTAIVNIHAGSCSSTT
IFDYKHGYIASRVLSRRACFILKMDHQNIPLNNLQWYIYEKQALDNMFSENKYTWVKYNPLE
SLIKDVDWFLLGSPIEKLCKHIPLYKGEVVENTHNVGAGGCAKAGLLGILGISICADIV

FIGURE 150

GGCACGAGCCAGGAAGTCTACTGCCCCGAGCAGAGGCCCTACACCCACCGAGGC
ATGGGGCTCCCTGGGCTGTTCTGCTTGGCCGTGCTGGCTGCCAGCAGCTTCTCCAAGGCACG
GGAGGAAGAAATTACCCCTGTGGTCTCCATTGCCTACAAAGTCTTGGAAGTTTTCCCCAAAG
GCCGCTGGGTGCTCATAACCTGCTGTGCACCCAGCCACCACCGCCCATCACCTATTCCCTC
TGTGGAACCAAGAACATCAAGGTGGCCAAGAAGGTGGTGAAGACCCACGAGCCGGCCTCCTT
CAACCTCAACGTCACTCAAGTCCAGTCCAGACCTGCTCACCTACTTCTGCCGGGCGTCCT
CCACCTCAGGTGCCCATGTGGACAGTGCCAGGCTACAGATGCACTGGGAGCTGTGGTCCAAG
CCAGTGTCTGAGCTGCGGGCCAACTTCACTCTGCAGGACAGAGGGGCAGGCCCCAGGGTGGA
GATGATCTGCCAGGCGTCCTCGGGCAGCCACCTATCACCAACAGCCTGATCGGGAAGGATG
GGCAGGTCCACCTGCAGCAGAGACCATGCCACAGGCAGCCTGCCAACTTCTCCTTCCTGCCG
AGCCAGACATCGGACTGGTTCTGGTGCCAGGCTGCAAACAACGCCAATGTCCAGCACAGCGC
CCTCACAGTGGTGCCCCCAGGTGGTGACCAGAAGATGGAGGACTGGCAGGGTCCCCTGGAGA
GCCCCATCCTTGCCCTTGCCGCTCTACAGGAGCACCCGCCGTCTGAGTGAAGAGGAGTTTGGG
GGGTTCAGGATAGGGAATGGGGAGGTGAGAGGACGCAAAGCAGCAGCCATGTAGAATGAACC
GTCCAGAGAGCCAAGCACGGCAGAGGACTGCAGGCCATCAGCGTGCACTGTTTCGTATTGGA
GTTTCATGCAAAATGAGTGTGTTTTAGCTGCTCTTGCCACAAAAAAAAAAAAAAAAAAAAA

FIGURE 151

MGLPGLFCLAVLAASSFSKAREEEITPVVSIAYKVLEVFPKGRWVLITCCAPQPPPPITYSL
CGTKNIKVAKKVVKTHEPASFNLNVTLMSSPDLLTYFCRASSTSGAHVDSARLQMHWELWSK
PVSELNANFTLQDRGAGPRVEMICQASSGSPPITNSLIGKDGQVHLQQRPCHRQPANFSFLP
SQTSDWFWCQAANNANVQHSALTVVPPGGDQKMEDWQGPLESPILALPLYRSTRRLSEEEFG
GFRIGNGEVRGRKAAAM

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FIGURE 152

GGTCCTTAATGGCAGCAGCCGCCGTACCAAGATCCTTCTGTGCCTCCCGCTTCTGCTCCTG
CTGTCCGGCTGGTCCCGGGCTGGGCGAGCCGACCCCTCACTCTCTTTGCTATGACATCACCGT
CATCCCTAAGTTCAGACCTGGACCACGGTGGTGTGCGGTTCAAGGCCAGGTGGATGAAAAGA
CTTTTCTTCACTATGACTGTGGCAACAAGACAGTCAACCTGTCAGTCCCCTGGGGAAGAAA
CTAAATGTCAACCGCCTGGAAAGCACAGAACCCAGTACTGAGAGAGGTGGTGGACATACT
TACAGAGCAACTGCGTGACATTCACTGGAGAATTACACACCCAAGGAACCCCTCACCTGC
AGGCAAGGATGTCTTGTGAGCAGAAAGCTGAAGGACACAGCAGTGGATCTTGGCAGTTCAGT
TTCGATGGGCAGATCTTCCTCCTCTTTGACTCAGAGAAGAGAATGTGGACAACGGTTCATCC
TGGAGCCAGAAAGATGAAAGAAAAGTGGGAGAATGACAAGGTTGTGGCCATGTCCTTCCATT
ACTTCTCAATGGGAGACTGTATAGGATGGCTTGAGGACTTCTTGATGGGCATGGACAGCACC
CTGGAGCCAAGTGCAGGAGCACCCTCGCCATGTCTCAGGCACAACCCAACTCAGGGCCAC
AGCCACCACCCTCATCCTTTGCTGCCTCCTCATCATCCTCCCCTGCTTCATCCTCCCTGGCA
TCTGAGGAGAGTCCTTTAGAGTGACAGGTTAAAGCTGATACCAAAAGGCTCCTGTGAGCAG
GTCTTGATCAAACCTCGCCCTTCTGTCTGGCCAGCTGCCCACGACCTACGGTGTATGTCCAGT
GGCCTCCAGCAGATCATGATGACATCATGGACCCAATAGCTCATTCACTGCCTTGATTCTTT
TTGCCAACAAATTTTACCAGCAGTTATACCTAACATATTATGCAATTTTCTCTTGGTGTACC
TGATGGAATTCCTGCACTTAAAGTTCCTGGCTGACTAAACAAGATATATCATTTTCTTTCTTC
TCTTTTTGTTTGGAAAATCAAGTACTTCTTTGAATGATGATCTCTTTCTTGCAAATGATATT
GTCAGTAAAATAATCACGTTAGACTTCAGACCTCTGGGGATTCTTTCCGTGTCCTGAAAGAG
AATTTTTAAATTATTTAATAAGAAAAAATTTATATTAAATGATTGTTTCCTTTAGTAATTTAT
TGTTCTGTACTGATATTTAAATAAAGAGTTCTATTTCCCAAAAAAAAAAAAAAAAAAAAA

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FIGURE 153

MAAAAATKILLCLPLLLLLSGWSRAGRADPHSLCYDITVIPKFRPGPRWCAVQGQVDEKTFL
HYDCGNKTVTPVSPPLGKKLNVTTAWKAQNPVLREVVDILTEQLRDIQLENYTPKEPLTLQAR
MSCEQKAEGHSSGSWQFSFDGQIFLLFDSEKRMWTTVHPGARKMKEKWENDKVVAMSFHYFS
MGDCIGWLEDFLMGMDSTLEPSAGAPLAMSSGTTQLRATATTLILCCLLIILPCFILPGI

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FIGURE 154

GGGAAAGCCATTTGAAAAACCCATCTATACAACTATATATTTTCATTTCTGCTGCTAGCTG
CCTTGGGCCTCACAATTTTCATTTCTGTTTTCTGACTTTCAAGTTATATACCGTGGAAATGGAG
TTGATCCCAACCATAACATCGTGGAGGGTTTTAATTTTGGTGGTAGCCCTCACCCAATTCTG
GTGTGGCTTTCTTTGCAGAGGATTCCACCTTCAAAATCATGAACTCTGGCTGTTGATCAAAA
GAGAATTTGGATTCTACTCTAAAAGTCAATATAGGACTTGGCAAAAGAAGCTAGCAGAAGAC
TCAACCTGGCCTCCCATAAACAGGACAGATTATTCAGGTGATGGCAAAAATGGATTCTACAT
CAACGGAGGCTATGAAAGCCATGAACAGATTCCAAAAAGAAAACCTCAAATTGGGAGGCCAAC
CCACAGAACAGCATTCTGGGCCAGGCTGTAATCAGAATTGTCGTCTACATGCTCAACAGC
ATTGCTTTTTTCCCCAAAATTAACACATTGTGGAGAAGTGATGATACTCTCCCCTTACCTTT
CCTCTCTCCATTCAAGCATTCAAAGTATATTTTCAATGAATTAAACCTTGCAGCAAGGGACC
TTAGATAGGCTTATTCTGACTGTATGCTTTACCAATGAGAGAAAAAAATGCATTTCTGTAT
CATCCTTTTCAATAAACTGTATTCAATTTGAAAAAAAAAAAAAAAAAAAAA

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FIGURE 155

MELIPTITSWRVLILVVALTQFW'CGFLCRGFHLQNHELWLLIKREFGFYSKSQYRTWQKKLA
EDSTWPPINRTDYSGDGKNGFYINGGYESHEQIPKRKLKLGQPTQHFWARL

FIGURE 156

GTTCCTCTTCCGAGCCAAAATCCCAGGCGATGGTGAATTATGAACGTGCCACACCATGAAG
CTCTTGTTGGCAGGTAACTGTGCACCACCACACCTGGAATGCCATCCTGCTCCCGTTCTGCTA
CCTCACGGCGCAAGTGTGGATTCTGTGTGCAGCCATCGCTGCTGCCGCCTCAGCCGGGCCCC
AGAACTGCCCCCTCCGTTTGTCTGTGCAGTAACCAGTTCAGCAAGGTGGTGTGCACGCGCCGG
GGCCTCTCCGAGGTCCCGCAGGGTATTCCCTCGAACACCCGGTACCTCAACCTCATGGAGAA
CAACATCCAGATGATCCAGGCCGACACCTTCCGCCACCTCCACCACCTGGAGGTCTGCACT
TGGGCAGGAACTCCATCCGGCAGATTGAGGTGGGGGCCCTTCAACGGCCTGGCCAGCCTCAAC
ACCTTGGAGCTGTTGACAACTGGCTGACAGTCATCCCTAGCGGGGCCCTTTGAATACCTGTC
CAAGCTGCGGGAGCTCTGGCTTCGCAACAACCCCATCGAAAGCATCCCCTCTTACGCCTTCA
ACCGGGTGCCCTCCCTCATGCGCTGGACTTGGGGGAGCTCAAGAAGCTGGAGTATATCTCT
GAGGGAGCTTTTGGGGGCTGTTCAACCTCAAGTATCTGAACTTGGGCATGTGCAACATTAA
AGACATGCCCAATCTCACCCCCCTGGTGGGGCTGGAGGAGCTGGAGATGTGAGGGAACCACT
TCCCTGAGATCAGGCCTGGCTCCTTCCATGGCCTGAGCTCCCTCAAGAAGCTCTGGGTATG
AACTCACAGGTCAGCCTGATTGAGCGGAATGCTTTTGACGGGCTGGCTTCACTTGTGGAAC
CAACTTGGCCCAATAACCTCTCTTCTTTGCCCCATGACCTCTTTACCCCGCTGAGGTACC
TGGTGGAGTTGCATCTACACCACAACCTTGGAACTGTGATTGTGACATTCTGTGGCTAGCC
TGGTGGCTTCGAGAGTATATACCCACCAATTCCACCTGCTGTGGCCGCTGTGATGCTCCCAT
GCACATGCGAGGCCGCTACCTCGTGGAGGTGGACCAGGCCTCCTTCCAGTGCTCTGCCCCCT
TCATCATGGACGCACCTCGAGACCTCAACATTTCTGAGGGTCGGATGGCAGAACTTAAGTGT
CGGACTCCCCCTATGTCTCTCCGTGAAGTGGTTGCTGCCCAATGGGACAGTGCTCAGCCACGC
CTCCCGCCACCCAAAGGATCTCTGTCTCTCAACGACGGCACCTTGAACTTTTCCACGTGCTGC
TTTCAGACACTGGGGTGTACACATGCATGGTGACCAATGTTGCAGGCAACTCCAACGCCTCG
GCCTACCTCAATGTGAGCACGGCTGAGCTTAACACCTCCAACCTACAGCTTCTTACCACAGT
AACAGTGGAGACCACGGAGATCTCGCCTGAGGACACAACGCGAAAGTACAAGCCTGTTCTTA
CCACGTCCACTGGTTACCAGCCGGCATATACCACCTCTACCACGGTGCTCATTACAGACTACC
CGTGTGCCCAAGCAGGTGGCAGTACCCGCGACAGACACCACTGACAAGATGCAGACCAGCCT
GGATGAAGTCATGAAGACCACCAAGATCATCATTGGCTGCTTTGTGGCAGTGACTCTGCTAG
CTGCCGCCATGTTGATTGTCTTCTATAAACTTCGTAAGCGGCACCAGCAGCGGAGTACAGTC
ACAGCCGCCCCGACTGTTGAGATAATCCAGGTGGACGAAGACATCCAGCAGCAACATCCGC
AGCAGCAACAGCAGCTCCGTCCGGTGTATCAGGTGAGGGGGCAGTAGTGCTGCCCACAATTC
ATGACCATATTAACACACCTACAAACCAGCACATGGGGCCCACTGGACAGAAAAACAGC
CTGGGGAACTCTCTGCACCCACAGTCACCACTATCTCTGAACCTTATATAATTAGACCCA
TACCAAGGACAAGGTACAGGAACTCAAATATGACTCCCCTCCCCCAAAAACTTATAAAAT
GCAATAGAATGCACACAAAGACAGCAACTTTTGTACAGAGTGGGGAGAGACTTTTCTTGTA
TATGCTTATATATTAAGTCTATGGGCTGGTTAAAAAAAACAGATTATATTAATAATTTAAAGA
CAAAAAGTCAAAAACA

FIGURE 157

MKLLWQVTVHHHTWNAILLPFVYLTAQVWILCAAIAAAAASAGPQNCPSVCSCSNQFSKVVCT
RRGLSEVPQGI PSNTRYLNL MENNIQMIQADTFRHLHHLEVLQLGRNSIRQIEVGAFNGLAS
LNTLELFDNWLTVIPSGAFEYLSKLRELWLRNNPIESIPSYAFNRVPSLMRLDLGELKKLEY
ISEGAFEGFLNLKYLNLGMCNIKDMPNLTPLVGLEELEMMSGNHFP EIRPGSFHGLSSLKKLW
VMNSQVSLIERNAFDGLASLVELNLAHNNLSSLP HDLFTPLRYLVELHLHHPWNCD CDILW
LAWWLREYIPTNSTCCGRCHAPMHMRGRYLVEVDQASFQCSAPFIMDAPRDLNISEGRMAEL
KCRTPPMSSVKWLLPNGTVLSHASRHPRI SVLNDGTLNFSHVLLSDTGVYTCMVTNVAGNSN
ASAYLNVSTAE LNTSNYSFFTTVTVETTEISPEDTTRKYKPVPTTSTGYQPAYTTSTTVLIQ
TTRVPKQVAVPATD TTDKMQTS LDEVMKTTKIIIGCFVAVTLLAAAMLIVFYKLRKRHQQRS
TVTAARTVEIIQVDEDIPAATSAAATAAPSGVSGEGAVVLPTIHDHINYNTYKPAHGAHWTE
NSLGNSLHPTVTTISEPYIIQHTKDKVQETQI

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FIGURE 158

CGCTCGGGCACCAGCCGCGGCAAGGATGAGCTGGGTGCTGGACGCAGTTGGGGCTCACTT
TTCTTCAGCTCCTTCTCATCTCGTCCCTGGCAAGAGAGTACACAGTCATTAATGAAGCCTGC
CCTGGAGCAGAGTGGAATATCATGTGTCGGGAGTGCTGTGAATATGATCAGATTGAGTGCGT
CTGCCCCGGAAGAGGGGAAGTCGTGGGTATACCATCCCTTGCTGCAGGAATGAGGAGAATG
AGTGTGACTCCTGCCTGATCCACCCAGGTTGTACCATCTTTGAAAAGCTGCAAGAGCTGCCGA
AATGGCTCATGGGGGGTACCTTGATGACTTCTATGTGAAGGGGTTCTACTGTGCAGAGTG
CCGAGCAGGCTGGTACGGAGGAGACTGCATGCGATGTGGCCAGGTTCTGCGAGCCCCAAAGG
GTCAGATTTTGTGGAAAGCTATCCCCTAAATGCTCACTGTGAATGGACCATTATGCTAAA
CCTGGGTTTGTCACTCAACTAAGATTTGTATGTTGAGTCTGGAGTTTGAATACATGTGCCA
GTATGACTATGTTGAGGTTTCGTGATGGAGACAACCGCATGGCCAGATCATCAAGCGTGTCT
GTGGCAACGAGCGGCCAGCTCCTATCCAGAGCATAGGATCCTCACTCCACGTCTCTCCAC
TCCGATGGCTCCAAGAATTTTGACGGTTTCCATGCCATTTATGAGGAGATCACAGCATGCTC
CTCATCCCCTTGTTCATGACGGCACGTGCGTCTTGACAAGGCTGGATCTTACAAGTGTG
CCTGCTTGGCAGGCTATACTGGGCAGCGCTGTGAAAATCTCCTTGAAGAAAGAAAGTCTCA
GACCCTGGGGGCCAGTCAATGGGTACCAGAAAATAACAGGGGGCCCTGGGCTTATCAACGG
ACGCCATGCTAAAATTGGCACCGTGGTGTCTTTCTTTTGTAACTCCTATGTTCTTAGTG
GCAATGAGAAAAGAACTTGCCAGCAGAATGGAGAGTGGTCAGGGAAACAGCCCATCTGCATA
AAAGCCTGCCGAGAACCAGATTTTCAAGCCTGGTGAGAAGGAGAGTCTTCCGATGCAGGT
TCAGTCAAGGGAGACACCATTACACCAGCTATACTCAGCGGCCTTCAAGCAGCAAGAACTGC
AGAGTGGCCCTACCAAGAAGCCAGCCCTTCCCTTTGGAGATCTGCCCATGGGATACCAACAT
CTGCATACCCAGCTCCAGTATGAGTGCATCTCACCCTTCTACCGCCGCTGGGCAGCAGCAG
GAGGACATGTCTGAGGACTGGGAAGTGGAGTGGGCGGGCACCATCCTGCATCCCTATCTGCG
GGAAAATTGAGAACATCACTGCTCCAAAGACCCAAGGGTTGCGCTGGCCGTGGCAGGCAGCC
ATCTACAGGAGGACCAGCGGGGTGCATGACGGCAGCCTACACAAGGGAGCGTGGTTCTAGT
CTGCAGCGGTGCCCTGGTGAATGAGCGCACTGTGGTGGTGGCTGCCCACTGTGTTACTGACC
TGGGGAAGGTCAACATGATCAAGACAGCAGACCTGAAAGTTGTTTTGGGGAAATTCTACCGG
GATGATGACCGGGATGAGAAGACCATCCAGAGCCTACAGATTTCTGCTATCATTCTGCATCC
CAACTATGACCCCATCCTGCTTGATGCTGACATCGCCATCCTGAAGCTCCTAGACAAGGCC
GTATCAGCACCCGAGTCCAGCCCATCTGCCTCGCTGCCAGTCGGGATCTCAGCACTTCTCTC
CAGGAGTCCCACATCACTGTGGCTGGCTGGAATGTCTTGGCAGACGTGAGGAGCCCTGGCTT
CAAGAACGACACACTGCGCTCTGGGGTGGTCACTGTGGTGGACTCGCTGCTGTGTGAGGAGC
AGCATGAGGACCATGGCATCCCAGTGAGTGTCACTGATAACATGTTCTGTGCCAGCTGGGAA
CCCACTGCCCCCTTCTGATATCTGCACTGCAGAGACAGGAGGCATCGCGGCTGTGTCTTCCC
GGGACGAGCATCTCCTGAGCCACGCTGGCATCTGATGGGACTGGTCACTGGAGCTATGATA
AAACATGCAGCCACAGGCTCTCCACTGCCTTACCAAGGTGCTGCCTTTTAAAGACTGGATT
GAAAGAAATATGAAATGAACCATGCTCATGCACTCCTTGAGAAGTGTCTGTATATCCGTC
TGTACGTGTGTCATTGCGTGAAGCAGTGTGGGCCTGAAGTGTGATTGGCCTGTGAACCTGG
CTGTGCCAGGGCTTCTGACTTCAGGGACAAAAGTCACTGAAGGGTGAGTAGACCTCCATTGC
TGGTAGGCTGATGCCGCTCCACTACTAGGACAGCCAATTGGAAGATGCCAGGGCTTGCAAG
AAGTAAGTTTCTTCAAAGAAGACCATATACAAAACCTCTCCACTCCACTGACCTGGTGGTCT
TCCCCAACTTTTCAAGTTATACGAATGCCATCAGCTTGACCAGGGAAGATCTGGGCTTCATGAG
GCCCCCTTTTGGAGGCTCTCAAGTTCTAGAGAGCTGCCTGTGGGACAGCCAGGGCAGCAGAGC
TGGGATGTGGTGATGCCTTTGTGTACATGGCCACAGTACAGTCTGGTCTTTTCTTCCCC
ATCTCTGTACACATTTTAAATAAAATAAGGGTTGGCTTCTGAACTACAAAAA
AA
AA

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FIGURE 159

MELGCWTQLGLTFLQLLLISSLPREYTVINEACPGAENIMCRECCEYDQIECVCPGKREVV
GYTIPCCRNEENECDSCLIHPGCTIFENCKSCRNGSWGGLDDFYVKGIFYCAECRAGWYGGD
CMRCGQVLRAPKGQILLESYPLNAHCEWTIHAKPGFVIQLRFVMLSLEFDYMCQYDYVEVRD
GDNRDGQIIKRVCGNERPAPIQSIGSSLHVLFHSDGSKNFDGFAIYEEITACSSSPCFHDG
TCVLDKAGSYKACLAGYTGQRCENLLEERNCSDPGGPVNGYQKITGGPGLINGRHAKIGTV
VSFFCNNSYVLSGNEKRTCQQNGEWSGKQPICIKACREPKISDLVRRRVLPQVQSRETPLH
QLYSAAFSKQKLQSAPTKKPALPFGDLPMGYQHLHTQLQYECISPFYRRLGSSRRTCLRTGK
WSGRAPSCIPICGKIENITAPKTQGLRWPWQAAIYRRTSGVHDGSLHKGAWFLVCSGALVNE
RTVVVAHCVTDLGKVMTIKTADLKVVVLGKFYRDDDRDEKTIQSLQISAIILHPNYDPILLD
ADIAILKLLDKARISTRVQPICLAASRDLSTSFQESHITVAGWNVLADVRSPGFKNDTLRSG
VVSVDSSLCEEQHEDHGIPVSVTDNMFCASWEPTAPSDICTAETGGIAAVSFPGRASPEPR
WHLMLVSWSYDKTCSHRLSTAFTKVL PFKDWIERNMK

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FIGURE 160

ACCAGGCATTGTATCTTCAGTTGTCATCAAGTTCGCAATCAGATTGGAAAAGCTCAACTTGA
AGCTTTCTTGCCCTGCAGTGAAGCAGAGAGATAGATATTATTACGTAATAAAAAACATGGGC
TTCAACCTGACTTTCCACCTTTCCTACAAATTCGATTACTGTTGCTGTTGACTTTGTGCCT
GACAGTGGTTGGGTGGGCCACCAGTAACCTTCGTGGGTGCCATTCAAGAGATTCTCTAAAG
CAAAGGAGTTTATGGCTAATTTCCATAAGACCCTCATTTTGGGGAAGGGAAAACTCTGACT
AATGAAGCATCCACGAAGAAGGTAGAACTTGACAACGTCTCTGTGTCTCCTTACCTCAG
AGGCCAGAGCAAGCTCATTTTCAAACCAGATCTCACTTTGGAAGAGGTACAGGCAGAAAATC
CCAAAGTGTCCAGAGGCCGGTATCGCCCTCAGGAATGTAAAGCTTTACAGAGGGTCGCCATCCTC
GTTCCCCACCGGAACAGAGAGAAACACCTGATGTACCTGCTGGAACATCTGCATCCCTTCCT
GCAGAGGCAGCAGCTGGATTATGGCATCTACGTATCCACCAGGCTGAAGGTAAAAAGTTTA
ATCGAGCCAACTCTTGAATGTGGGCTATCTAGAAGCCCTCAAGGAAGAAAATTGGGACTGC
TTTATATTCCACGATGTGGACCTGGTACCCGAGAATGACTTTAACCTTTACAAGTGTGAGGA
GCATCCCAAGCATCTGGTGGTTGGCAGGAACAGCACTGGGTACAGGTTACGTTACAGTGGAT
ATTTTGGGGGTGTTACTGCCCTAAGCAGAGAGCAGTTTTTCAAGGTGAATGGATTCTCTAAC
AACTACTGGGGATGGGGAGGCGAAGACGATGACCTCAGACTCAGGGTTGAGCTCCAAAGAAT
GAAAATTTCCCGGCCCTGCCTGAAGTGGGTAAATATACAATGGTCTTCCACACTAGAGACA
AAGGCAATGAGGTGAACGCAGAACGGATGAAGCTCTTACACCAAGTGTACAGAGTCTGGAGA
ACAGATGGGTTGAGTAGTTGTTCTTATAAATTAGTATCTGTGGAACACAATCCTTTATATAT
CAACATCACAGTGGATTTCTGGTTTGGTGCATGACCCTGGATCTTTTGGTGATGTTTGGAAAG
AACTGATTCTTTGTTTGCAATAATTTTGGCCTAGAGACTTCAAATAGTAGCACACATTAAGA
ACCTGTTACAGCTCATTGTTGAGCTGAATTTTTCTTTTTGTATTTCTTAGCAGAGCTCCT
GGTGATGTAGAGTATAAACAGTTGTAACAAGACAGCTTTCTTAGTCATTTTGATCATGAGG
GTTAAATATTGTAATATGGATACTTGAAGGACTTTATATAAAAGGATGACTCAAAGGATAAA
ATGAACGCTATTTGAGGACTCTGGTTGAAGGAGATTTATTTAAATTTGAAGTAATATATTAT
GGGATAAAAGGCCACAGGAAATAAGACTGCTGAATGTCTGAGAGAACCAGAGTTGTTCTCGT
CCAAGGTAGAAAGGTACGAAGATACAATACTGTTATTATTTATCCTGTACAATCATCTGTG
AAGTGGTGGTGTGAGGTGAGAAGGCGTCCACAAAAGAGGGGAGAAAAGGCGACGAATCAGGA
CACAGTGAACCTTGGGAATGAAGAGGTAGCAGGAGGGTGGAGTGTGGCTGCAAAGGCAGCAG
TAGCTGAGCTGGTTGCAGGTGCTGATAGCCTTCAGGGGAGGACCTGCCCAGGTATGCCTTCC
AGTGATGCCCACCAGAGAATACATTCTCTATTAGTTTTTAAAGAGTTTTTGTAAAATGATTT
TGTACAAGTAGGATATGAATTAGCAGTTTACAAGTTTACATATTAATAATAATAATATGT
CTATCAAATACCTCTGTAGTAAATGTGAAAAGCAAAA

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FIGURE 161

MGFNLTfHLSYKFRLLLLLTLCITVVGWATSNYFVGAIQEIPKAKEFMANFHKTLLLGKGKT
LTNEASTKKVELDNCPSVSPYLRGQSKLIFKPDLTLEEVQAENPKVSRGRYRPQECKALQRV
AILVPHRNREKHLMYLLEHLHPFLQRQQLDYGIYVIHQAEKKFNRAKLLNVGYLEALKEEN
WDCFIFHDVDLVPENDFNLYKCEEHPKHLVVGRNSTGYRLRYSGYFGGVTALSREQFFKVNG
FSNNYWGWWGEGDDDLRLRVELQRMKISRPLPEVGKYTMVFHTRDKGNEVNAERMKLLHQVSR
VWRTDGLSSCSYKLVSVEHNPLYINITVDFWFGA

Important features:

Signal peptide:

amino acids 1-27

N-glycosylation sites:

amino acids 4-7, 220-223 and 335-338

Xylose isomerase proteins:

amino acids 191-201

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FIGURE 162

CGTGGGCCGGGGTTCGCGCAGCGGGCTGTGGGCGCGCCCGAGGAGCGACCGCCGAGTTCTC
GAGCTCCAGCTGCATTCCCTCCGCGTCCGCCCCACGCTTCTCCCGCTCCGGGCCCCGCAATG
GCCCAGGCAGTGTGGTTCGCGCCTCGGCGCATCCTCTGGCTTGCTGCTCCTGCCCTGGGC
CCCGGCAGGGGTGGCCGAGGCCTGTATGAACTCAATCTCACCACCGATAGCCCTGCCACCA
CGGGAGCGGTGGTGACCATCTCGGCCAGCCTGGTGGCCAAGGACAACGGCAGCCTGGCCCTG
CCCGCTGACGCCCACCTCTACCGCTTCCACTGGATCCACACCCCGCTGGTGCTTACTGGCAA
GATGGAGAAGGGTCTCAGCTCCACCATCCGTGTGGTTCGGCCACGTGCCCGGGGAATTCCCGG
TCTCTGTCTGGGTCACTGCCGCTGACTGCTGGATGTGCCAGCCTGTGGCCAGGGGCTTTGTG
GTCTCCCCATCACAGAGTTCTCGTGGGGGACCTTGTTGTACCCAGAACACTTCCCTACC
CTGGCCAGCTCCTATCTCACTAAGACCGTCTGAAAGTCTCCTTCTCTCCACGACCCGA
GCAACTTCTCAAGACCGCCTTGTCTCTCTACAGCTGGGACTTCGGGGACGGGACCCAGATG
GTGACTGAAGACTCCGTGGTCTATTATAACTATTCCATCATCGGGACCTTCACCGTGAAGCT
CAAACTGCTGGCGGAGTGGGAAGAGGTGGAGCCGGATGCCACGAGGGCTGTGAAGCAGAAGA
CCGGGGACTTCTCCGCTCGCTGAAGCTGCAGGAAACCTTCGAGGCATCCAAGTGTGGGG
CCCACTTAATTGAGACCTTCCAAAAGATGACCGTGACCTTGAAGTCTCTGGGGAGCCCTCC
TCTGACTGTGTGCTGGCGTCTCAAGCCTGAGTGCCTCCCGCTGGAGGAAGGGGAGTGCCACC
CTGTGTCCGTGGCCAGCACAGCGTACAACCTGACCCACACCTTCAGGGACCTTGGGGACTAC
TGCTTCAGCATCCGGGCGGAGAATATCATCAGCAAGACACATCAGTACCACAAGATCCAGGT
GTGGCCCTCCAGAATCCAGCCGGCTGTCTTGTCTTCCCATGTGCTACACTTATCACTGTGA
TGTTGGCCTTCATCATGTACATGACCTGCGGAATGCCACTCAGCAAAAAGGACATGGTGGAG
AACCCGGAGCCACCTCTGGGGTCAAGTGTGCTGCCAGATGTGCTGTGGGCCCTTCTTGCT
GGAGACTCCATCTGAGTACCTGGAAATTGTTCTGTGAGAACCACGGGCTGCTCCCGCCCTCT
ATAAGTCTGTCAAACTTACACCGTGTGAGCACTCCCCCTCCCCACCCATCTCAGTGTTAA
CTGACTGCTGACTTGGAGTTTCCAGCAGGGTGGTGTGCACCACTGACCAGGAGGGGTTCAAT
TGCGTGGGGCTGTTGGCCTGGATCATCCATCCATCTGTACAGTTCAAGCACTGCCACAAGCC
CCTCCCTCTCTGTACCCCTGACCCAGCCATTACCCATCTGTACAGTCCAGCCACTGACA
TAAGCCCCACTCGGTTACCACCCCTTGACCCCTACCTTTGAAGAGGCTTCGTGCAGGACT
TTGATGCTTGGGGTGTTCCTGTGACTCCTAGGTGGGCCTGGCTGCCCACTGCCCATTCCT
CTCATATTGGCACATCTGCTGTCCATTGGGGGTCTCAGTTTCTCCCCCAGACAGCCCTAC
CTGTGCCAGAGAGCTAGAAAGAAGGTCTAAAGGGTTAAAAATCCATAACTAAAGGTTGTAC
ACATAGATGGGCACACTCACAGAGAGAAGTGTGCATGTACACACACCACACACACACACA
CACACACACACAGAAATATAAACACATGCGTCACATGGGCATTTCAAGATGATCAGCTCTGTA
TCTGGTTAAGTCGGTTGCTGGGATGCACCCTGCACTAGAGCTGAAAGGAAATTTGACCTCCA
AGCAGCCCTGACAGGTTCTGGGCCCGGGCCCTCCCTTTGTGCTTTGTCTCTGCAGTTCTTGC
GCCCTTTATAAGGCCATCCTAGTCCCTGCTGGCTGGCAGGGGCTGGATGGGGGGCAGGACT
AATACTGAGTGATTGCAGAGTGCTTTATAAAATATCACCTTATTTTATCGAAACCCATCTGTG
AAACTTTCACTGAGGAAAAGGCCTTGACGCGGTAGAAGAGGTTGAGTCAAGGCCGGCGCGG
TGGCTCACGCCTGTAATCCAGCACTTTGGGAGGCCGAGGCGGGTGGATCACGAGATCAGGA
GATCGAGACCACCTGGCTAACACGGTGAAACCCCGTCTCTACTAAAAAAATACAAAAAGTT
AGCCGGGCGTGGTGGTGGTGCCTGTAGTCCAGCTACTCGGGAGGCTGAGGCAGGAGAATG
GTGCGAACCCGGGAGGCGGAGCTTGCAGTGAGCCAGATGGCGCCACTGCACTCCAGCCTGA
GTGACAGAGCGAGACTCTGTCTCCA

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FIGURE 163

MAQAVWSRLGRILWLACLLPWAPAGVAAGLYELNLTTDSPATTGAVVTISASLVAKDNGSLA
LPADAHLYRFHWIHTPLVLTGKMEKGLSSTIRVVGHPGEFPVSVWVTAADCWMCQPVARGF
VVLPITEFLVGDLVVTQNTSLPWPSYLTCTVLKVSFLLHDPSNFLKTALFLYSWDFGDGTQ
MVTEDSVVYYNYSIIIGTFTVKLKVVAEWEEVEPDATRAVKQKTGDFSASLKLQETLRGIQVL
GPTLIQTFQKMTVTNLNFGSPPLTVCWRLKPECLPLEEGECHPVSVASTAYNLTHTRDPGD
YCFSIRAENIISKTHQYHKIQVWPSRIQPAVFAPPCATLITVMLAFIMYMTLRNATQQKDMV
ENPEPPSGVRCCCOMCCGPFLLETPSEYLEIVRENHGLLPPLYKSVKTYTV

Important features of the protein:

Signal peptide:

amino acids 1-24

Transmembrane domain:

amino acids 339-362

N-glycosylation sites.

amino acids 34-37, 58-61, 142-145, 197-200, 300-303 and 364-367

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FIGURE 165

MASSQIWAACLLLLLLASLTSCSVFPQQTGQLAELQPQDRAGARASWMPMFQRRRRRDTH
FPICIFCCGCCHRSKCGMCCKT

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FIGURE 166

CTGT CAGGAAGGACCATCTGAAGGCTGCAATTTGTTCTTAGGGAGGCAGGTGCTGGCCTGGC
CTGGATCTTCCACCAATGTTTCCTGTTGCTGCCTTTTGATAGCCTGATTGTCAACCTTCTGGGC
ATCTCCCTGACTGTCTCTTACCCCTCCTTCTCGTTTTCATCATAGTGCCAGCCATTTTGG
AGTCTCCTTTGGTATCCGCAAACTCTACATGAAAAGTCTGTTAAAAATCTTGGCTGGGCTA
CCTTGAGAATGGAGCGAGGAGCCAAGGAGAAGAACCACCAGCTTTACAAGCCCTACACCAAC
GGAATCATTGCAAAGGATCCCACTTCACTAGAAGAAGAGATCAAAGAGATTCTCGTGAAGTGG
TAGTAGTAAGGCTCTGGACAACACTCCAGAGTTCGAGCTCTCTGACATTTTCTACTTTTGGC
GGAAAGGAATGGAGACCATTATGGATGATGAGGTGACAAAGAGATTCTCAGCAGAAGAACTG
GAGTCTTGGAACCTGCTGAGCAGAACCAATTATAACTTCCAGTACATCAGCCTTTCGGCTCAC
GGTCTGTGGGGGTTAGGAGTGTGATTTCGGTACTGCTTTCTGCTGCCGCTCAGGATAGCAC
TGGCTTTTACAGGGATTAGCCTTCTGGTGGTGGGCACAACTGTGGTGGGATACTTGCCAAAT
GGGAGGTTTAAAGGAATTCATGAGTAAACATGTTCACTTAATGTGTTACCGGATCTCGGTGCG
AGCGCTGACAGCCATCATCACCTACCATGACAGGGAAAACAGACCAAGAAATGGTGGCATCT
GTGTGGCCAATCATACCTCACCGATCGATGTGATCATCTTGGCCAGCGATGGCTATTATGCC
ATGGTGGGTCAAGTGCACGGGGGACTCATGGTGTGATTTCAGAGAGCCATGGTGAAGGCCGTG
CCCACACGTCTGTTTTGAGCGCTCGGAAGTGAAGGATCGCCACCTGGTGGCTAAGAGACTGA
CTGAACATGTGCAAGATAAAAGCAAGCTGCCTATCCTCATCTTCCCAGAAGGAACCTGCATC
AATAATACATCGGTGATGATGTTCAAAAAGGGAAGTTTTGAAATTGGAGCCACAGTTTACCC
TGTTGCTATCAAGTATGACCCTCAATTTGGCGATGCCTTCTGGAACAGCAGCAAATACGGGA
TGGTGACGTACCTGCTGCGAATGATGACCAGCTGGGCCATTGTCTGCAGCGTGTGGTACCTG
CCTCCCATGACTAGAGAGGCAGATGAAGATGCTGTCCAGTTTTCGAATAGGGTGAAATCTGC
CATTGCCAGGCAGGGAGGACTTGTGGACCTGCTGTGGGATGGGGCCCTGAAGAGGGAGAAGG
TGAAGGACACGTTCAAGGAGGAGCAGCAGAAGCTGTACAGCAAGATGATCGTGGGGAACAC
AAGGACAGGAGCCGCTCCTGAGCCTGCCTCCAGCTGGCTGGGGCCACCGTGCGGGGTGCCAA
CGGGCTCAGAGCTGGAGTTGCCGCCGCCGCCCTGCTGTGTCTTTCCAGACTCCAGGG
CTCCCCGGGCTGCTCTGGATCCCAGGACTCCGGCTTTCGCCGAGCCGCAGCGGGATCCCTGT
GCACCCGGCGCAGCCTACCTTGGTGGTCTAAACGGATGCTGCTGGGTGTTGCGACCCAGGA
CGAGATGCCTTGTTTCTTTTACAATAAGTCGTTGGAGGAATGCCATTAAAGTGAACCTCCCA
CCTTTGCACGCTGTGCGGGCTGAGTGGTTGGGGAGATGTGGCCATGGTCTTGTGCTAGAGAT
GGCGGTACAAGAGTCTGTTATGCAAGCCCGTGTGCCAGGGATGTGCTGGGGGCGGCCACCCG
CTCTCCAGGAAAGGCACAGCTGAGGCACTGTGGCTGGCTTCGGCCTCAACATCGCCCCCAGC
CTTGGAGCTCTGCAGACATGATAGGAAGGAACTGTCATCTGCAGGGGCTTTTTCAGCAAAATG
AAGGGTTAGATTTTTATGCTGCTGCTGATGGGGTTACTAAAGGGAGGGGAAGAGGCCAGGTG
GGCCGCTGACTGGGCCATGGGGAGAACGTGTGTTCTGACTCCAGGCTAACCTGAACTCCCC
ATGTGATGCGCGCTTTGTTGAATGTGTGTCTCGGTTTCCCCATCTGTAATATGAGTCGGGGG
GAATGGTGGTGATTCCCTACCTCACAGGGCTGTTGTGGGGATTAAAGTGTGCGGGTGAGTGA
AGGACACATCACGTTTCAGTGTTCAGGTACAGGCCCAAAAACGGGGCACGGCAGGCCCTGAG
CTCAGAGCTGCTGCACTGGGCTTTGGATTTGTTCTTGTGAGTAAATAAACTGGCTGGTGAATGA

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FIGURE 167

MFLLLPFDSLIVNLDGISLTIVLFTLLLVFTIIVPAIFGVSFGLRKLKLYMKSLLKIFAWATLRME
RGAKEKNHQLYKPYTNGIIAKDPTSLEEEIKEIRRSKSSKALDNTPEFELSDIFYFCRKGME
TIMDDEVTKRFSAEELSWNLLSRTNYNFYISLRLTVLWGLGVLI RYCFLLPLRIALAF TG
ISLLVVGTTVVGYLPNGRFKEFMSKHVHLMCYRICVRALTAIITYHDRENRPNGGICVANH
TSPIDVIIILASDGYAMVGQVHGGLMGVIQAMVKACPHVWFERSEVKDRHLVAKRLTEHVQ
DKSKLPILIFPEGTCINNTSVMMFKKGSFEIGATVYPVAIKYDPQFGDAFWNSSKYGMV TYL
LRMTSWAIVCSVWYLPMTREADEDAVQFANRVKSAIARQGGLVDLLWDGGLKREKVKDTF
KEEQKLYSKMIVGNHKDRSRS

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FIGURE 168

GCCCCTCGAAACAGGACTCCAGCACCTCTGGTCCCCGCCCTCACCCGGACCCCTGGCCCTCA
CGTCTCCTCCAGGGATGGCGCTGGCGGCTTTGATGATCGCCCTCGGCAGCCTCGGCCTCCAC
ACCTGGCAGGCCCAGGCTGTTCCACCATCCTGCCCCCTGGGCCTGGCTCCAGACACCTTTGA
CGATACCTATGTGGGTTGTGCAGAGGAGATGGAGGAGAAGGCAGCCCCCTGCTAAAGGAGG
AAATGGCCCACCATGCCCTGCTGCCGGAATCCTGGGAGGCAGCCAGGAGACCTGGGAGGAC
AAGCGTCGAGGGCTTACCTTGCCCCCTGGCTTCAAAGCCCAGAATGGAATAGCCATTATGGT
CTACACCAACTCATCGAACACCTTGTACTGGGAGTTGAATCAGGCCGTGCGGACGGGCGGAG
GCTCCCGGGAGCTCTACATGAGGCACCTTCCCTTCAAGGCCCTGCATTTCTACCTGATCCG
GCCCTGCAGCTGCTGCGAGGCAGTGGGGGCTGCAGCAGGGGACCTGGGGAGGTGGTGTTCG
AGGTGTGGGCAGCCTTCGCTTTGAACCCAAGAGGCTGGGGGACTCTGTCCGCTTGGGCCAGT
TTGCCTCCAGCTCCCTGGATAAAGCAGTGGCCACAGATTTGGGGAGAAGAGGCGGGGCTGT
GTGTCTGCGCCAGGGGTGCAGCTAGGGTCACAATCTGAGGGGGCCTCCTCTCTGCCCCCTG
GAAGACTCTGCTCTTGGCCCCCTGGAGAGTTCCAGCTCTCAGGGGTGGGGCCCTGAAAGTCCA
ACATCTGCCACTTAGGAGCCCTGGGAACGGGTGACCTTCATATGACGAAGAGGCACCTCCAG
CAGCCTTGAGAAGCAAGAACATGGTTCCGGACCCAGCCCTAGCAGCCTTCTCCCCAACCCAGG
ATGTTGGCCTGGGGAGGCCACAGCAGGGCTGAGGGAACCTCTGCTATGTGATGGGGACTTCCT
GGGACAAGCAAGGAAAGTACTGAGGCAGCCACTTGATTGAACGGTGTTGCAATGTGGAGACA
TGGAGTTTTATTGAGGTAGCTACGTGATTAAATGGTATTGCAGTGTGGA

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FIGURE 169

MALAALMIALGSLGLHTWQAQAVPTILPLGLAPDTFDDTYVGCAEEMEEKAAPLLKEEMAHH
ALLRESWEAAQETWEDKRRGLTLPPGFKAQNGIAIMVYTNSSNTLYWELNQAVRTGGGSREL
YMRHFFKALHFYLIRALQLLRGSGGCSRGPGEVVFRGVGSLRFEPKRLGDSVRLGQFASSS
LDKAVAHRFGEKRRGCVSAPGVQLGSQSEGASSLPPWKTLLLAPGEFQLSGVGP

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FIGURE 170

GTGGCTTCATTTTCAGTGGCTGACTTCCAGAGAGCAATATGGCTGGTTCCCCAACATGCCTCA
CCCTCATCTATATCCTTTGGCAGCTCACAGGGTCAGCAGCCTCTGGACCCGTGAAAGAGCTG
GTCGGTTCCGTTGGTGGGGCCGTGACTTTCCCCCTGAAGTCCAAAGTAAAGCAAGTTGACTC
TATTGTCTGGACCTTCAACACAACCCCTCTTGTCAACCATAAGCCAGAGGGGGGCACTATCA
TAGTGACCCAAAATCGTAATAGGGAGAGAGTAGACTTCCCAGATGGAGGCTACTCCCTGAAG
CTCAGCAAACCTGAAGAAGAATGACTCAGGGATCTACTATGTGGGGATATACAGCTCATCACT
CCAGCAGCCCTCCACCCAGGAGTACGTGCTGCATGTCTACGAGCACCTGTCAAAGCCTAAAG
TCACCATGGGTCTGCAGAGCAATAAGAATGGCACCTGTGTGACCAATCTGACATGCTGCATG
GAACATGGGGAAGAGGATGTGATTTATACCTGGAAGGCCCTGGGGCAAGCAGCCAATGAGTC
CCATAATGGGTCCATCCTCCCCATCTCCTGGAGATGGGGAGAAAGTGATATGACCTTCATCT
GCGTTGCCAGGAACCCTGTCAGCAGAACTTCTCAAGCCCCATCCTTGCCAGGAAGCTCTGT
GAAGGTGCTGCTGATGACCCAGATTCCCTCCATGGTCCTCCTGTGTCTCCTGTTGGTGGCCCT
CCTGCTCAGTCTCTTTGTACTGGGGCTATTTCTTTGGTTTCTGAAGAGAGAGAGACAAGAAG
AGTACATTGAAGAGAAGAAGAGAGTGGACATTTGTGCGGAAACTCCTAACATATGCCCCCAT
TCTGGAGAGAACACAGAGTACGACACAATCCCTCACACTAATAGAACAATCCTAAAGGAAGA
TCCAGCAAATACGGTTTACTCCACTGTGGAAATACCGAAAAAGATGGAAAATCCCCACTCAC
TGCTCACGATGCCAGACACACCAAGGCTATTTGCCTATGAGAATGTTATCTAGACAGCAGTG
CACTCCCCTAAGTCTCTGCTCA

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FIGURE 171

MAGSPTCLTLIYILWQLTGSAASGPVKELVGSVGGAVTFPLKSKVKQVDSIVWTFNTTPLVT
IQPEGGTIIIVTQNRNRERVDFPDGGYSLKLSKLKKNDSGIYYVGIYSSSLQQPSTQEYVLHV
YEHLSPKVTMGLQSNKNGTCVTNLTCMEHGEEDVIYTWKALGQAANESHNGSILPISWRW
GESDMTFICVARNPVSRNFSSPILARKLCEGAADDPDSSMVLLCLLLVPLLLSLFVLGLFLW
FLKRERQEEYIEKKRVDICRETPNICPHSGENTYDTIPHTNRTILKEDPANTVYSTVEIP
KKMENPHSLLTMPDTPRLFAYENVI

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FIGURE 172

CTGGTTCCCCAACATGCCTCACCCCTCATCTATATCCTTTGGCAGCTCACAGGGTCAGCAGCC
TCTGGACCCCGTGAAAGAGCTGGTCCGTTCCGTTGGTGGGGCCGTGACTTTCCCCCTGAAGTC
CAAAGTAAAGCAAGTTGACTCTATTGTCTGGACCTTCAACACAACCCCTCTTGTCACCATAC
AGCCAGAAGGGGGCACTATCATAGTGACCCAAAATCGTAATAGGGAGAGAGTAGACTTCCCA
GATGGAGGGCTACTCCCTGAAGCTCAGCAAACCTGAAGAAGAATGACTCAGGGATCTACTATGT
GGGGATATACAGCTCATCACTCCAGCAGCCCTCCACCCAGGAGTACGTGCTGCATGTCTACG
AGCACCTGTCAAAGCCTAAAGTCACCATGGGTCTGCAGAGCAATAAGAATGGCACCTGTGTG
ACCAATCTGACATGCTGCATGGAACATGGGGAAGAGGATGTGATTTATACCTGGAAGGCCCT
GGGGCAAGCAGCCAATGAGTCCCATAATGGGTCCATCCTCCCCATCTCCTGGAGATGGGGAG
AAAGTGATATGACCTTCATCTGCGTTGCCAGGAACCCTGTCAGCAGAAAACCTCTCAAGCCCC
ATCCTTGCCAGGAAGCTCTGTGAAGGTGCTGCTGATGACCCAGATTCTCCATGGTCTCTCT
GTGTCTCCTGTTGGTGCCCCCTCCTGCTCAGTCTCTTTGTAAGTGGGGCTATTTCTTTGGTTTC
TGAAGAGAGAGAGACAAGAAGAGTACATTGAAGAGAAGAAGAGAGTGGACATTTGTCTGGGAA
ACTCCTAACATATGCCCCCATCTGGAGAGAACACAGAGTACGACACAATCCCTCACACTAA
TAGAACAATCCTAAAGGAAGATCCAGCAAATACGGTTTACTCCACTGTGGAAATACCGAAAA
AGATGGAAAATCCCCACTCACTGCTCACGATGCCAGACACACCAAGGCTATTTGCCTATGAG
AATGTTATCTAGACAGCAGTGCACTCCCCTAAGTCTCTGCTCAAAAAAAAAAAAAAAAAAAAA

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FIGURE 173

GAAAGACGTGGTCCTGACAGACAGACAATCCTATTCCCTACCAAAATGAAGATGCTGCTGCT
GCTGTGTTTGGGACTGACCCTAGTCTGTGTCCATGCAGAAGAAGCTAGTTCTACGGGAAGGA
ACTTTAATGTAGAAAAGATTAATGGGGAATGGCATACTATTATCCTGGCCTCTGACAAAAGA
GAAAAGATAGAAGAACATGGCAACTTTAGACTTTTTCTGGAGCAAATCCATGTCTTGAGAA
TTCCTTAGTTCTTAAAGTCCATACTGTAAGAGATGAAGAGTGCTCCGAATTATCTATGGTTG
CTGACAAAACAGAAAAGGCTGGTGAATATTCTGTGACGTATGATGGATTCAATACATTTACT
ATACCTAAGACAGACTATGATAACTTTCTTATGGCTCACCTCATTAACGAAAAGGATGGGGA
AACCTTCCAGCTGATGGGGCTCTATGGCCGAGAACCAGATTTGAGTTCAGACATCAAGGAAA
GGTTTGCACACTATGTGAGGAGCATGGAATCCTTAGAGAAAATATCATTGACCTATCCAAT
GCCAATCGCTGCCTCCAGGCCCAGAAATGAAGAATGGCCTGAGCCTCCAGTGTTGAGTGAC
ACTTCTCACCAGGACTCCACCATCATCCCTTCCTATCCATACAGCATCCCCAGTATAAATTC
TGTGATCTGCATTCCATCCTGTCTCACTGAGAAGTCCAATTCAGTCTATCAACATGTTACC
TAGGATACCTCATCAAGAATCAAAGACTTCTTTAAATTTCTCTTTGATACACCCTTGACAAT
TTTTCATGAAATTATTCCTCTTCCTGTTCAATAAATGATTACCCTTGCACTTAA

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FIGURE 174

MKMLLLLCLGLTLVCVHAEASSTGRNFNVEKINGEWHTIILASDKREKIEEHGNFRLFLEQ
IHVLENSLVLVKVTVRDEECSELSMVADKTEKAGEYSVTYDGFNTFTIPKTDYDNFLMAHLI
NEKDGETFQLMGLYGREPDLSSEIKERFAQLCEEHGILRENIIDLSNANRCLQARE

[illegible]

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FIGURE 176

MTCCEGWTSCNGFSLLVLLLLGVVLNAIPLIVSLVEEDQFSQNPISCFEWWFPGIIGAGLMA
IPATTMSLTARKRACCNNRTGMFLSSFFSVITVIGALYCMLISIQALLKGPLMCNPSNSNA
NCEFSLKNISDIHPESFNLQWFFNDSCAPPTGFNKPTSNDTMASGWRASSFHFDFSEENKHRL
IHFSVFLGLLLVGILEVLFGLSQIVIGFLGCLCGVSKRRSQIV

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FIGURE 177

GTCGAATCCAAATCACTCATTGTGAAAGCTGAGCTCACAGCCGAATAAGCCACCAATGAGGCT
GTCAGTGTGTCTCCTGATGGTCTCGCTGGCCCTTTGCTGCTACCAGGCCCATGCTCTTGTCT
GCCCAGCTGTTGCTTCTGAGATCACAGTCTTCTTATTCTTAAGTGACGCTGCGGTAAACCTC
CAAGTTGCCAAACTTAATCCACCTCCAGAAGCTCTTGCAGCCAAGTTGGAAGTGAAGCACTG
CACCGATCAGATATCTTTTAAGAAACGACTCTCATTGAAAAAGTCCTGGTGGAAAATAGTGAA
AAAATGTGGTGTGTGACATGTAAAAATGCTCAACCTGGTTTCCAAAGTCTTTCAACGACACC
CTGATCTTCACTAAAAATTGTAAAGGTTTCAACACGTTGCTTTAATAAATCACTTGCCCTGC

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FIGURE 178

MRLSVCLLMVSLALCCYQAHALVCPAVASEITVFLFLSDAAVNLQVAKLNPPPEALAAKLEV
KHCTDQISFKKRLSLKKSWWK

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FIGURE 179

ATCCGTTCTCTGCGCTGCCAGCTCAGGTGAGCCCTCGCCAAGGTGACCTCGCAGGACACTGG
TGAAGGAGCAGTGAGGAACCTGCAGAGTCACACAGTTGCTGACCAATTGAGCTGTGAGCCTG
GAGCAGATCCGTGGGCTGCAGACCCCCGCCCCAGTGCCTCTCCCCCTGCAGCCCTGCCCCCTC
GAACTGTGACATGGAGAGAGTGACCCTGGCCCTTCTCCTACTGGCAGGCCTGACTGCCTTGG
AAGCCAATGACCCATTTGCCAATAAAGACGATCCCTTCTACTATGACTGGAAAAACCTGCAG
CTGAGCGGACTGATCTGCGGAGGGCTCCTGGCCATTGCTGGGATCGCGGCAGTTCTGAGTGG
CAAATGCAAATACAAGAGCAGCCAGAAGCAGCACAGTCCTGTACCTGAGAAGGCCATCCCAC
TCATCACTCCAGGCTCTGCCACTACTTGCTTGAGCACAGGACTGGCCTCCAGGGATGGCCTGA
AGCCTAACACTGGCCCCCAGCACCTCCTCCCCGGGAGGCCTTATCCTCAAGGAAGGACTTC
TCTCCAAGGGCAGGCTGTTAGGCCCTTTCTGATCAGGAGGCTTCTTTATGAATTAAACTCG
CCCCACCACCCCTCA

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FIGURE 180

MERVTLALLLLAGLTALEANDPFANKDDPFYYDWKNLQLSGLICGGLLAIAAGIAAVLSGKCK
YKSSQKQHSPVPEKAIPILITPGSATTC

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FIGURE 181

GGAGAAGAGGTTGTGTGGGACAAGCTGCTCCCGACAGAAGGATGTCGCTGCTGAGCCTGCCC
TGGCTGGGCCTCAGACCGGTGGCAATGTCCCCATGGCTACTCCTGCTGCTGGTTGTGGGCTC
CTGGCTACTCGCCCGCATCCTGGCTTGGACCTATGCCTTCTATAACAACTGCCGCCGGCTCC
AGTGTTTCCACAGCCCCCAAACGGAACTGGTTTTGGGGTCACCTGGGCCTGATCACTCCT
ACAGAGGAGGGCTTGAAGGACTCGACCCAGATGTGGCCACCTATTCCAGGGCTTTACGGT
ATGGCTGGGTCCCATCATCCCCTTCATCGTTTTATGCCACCCTGACACCATCCGGTCTATCA
CCAATGCCTCAGCTGCCATTGCACCCAAGGATAATCTCTTCATCAGGTTCTGAAGCCCTGG
CTGGGAGAAGGGATACTGCTGAGTGGCGGTGACAAGTGGAGCCGCCACCGTCGGATGCTGAC
GCCCCCCTTCCATTTCAACATCCTGAAGTCCTATATAACGATCTTCAACAAGAGTGCAACA
TCATGCTTGACAAGTGGCAGCACCTGGCCTCAGAGGGCAGCAGTCGTCTGGACATGTTTGAG
CACATCAGCCTCATGACCTTGGACAGTCTACAGAAATGCATCTTCAGCTTTGACAGCCATTG
TCAGGAGAGGCCAGTGAATATATTGCCACCATCTTGGAGCTCAGTGCCCTTGAGAGAAAA
GAAGCCAGCATATCCTCCAGCACATGGACTTTCTGTATTACCTCTCCCATGACGGGCGGCGC
TTCCACAGGGCCTGCCGCTGGTGCATGACTTCACAGACGCTGTATCCGGGAGCGGCGTCCG
CACCTCCCCACTCAGGGTATTGATGATTTTTTCAAAGACAAAGCCAAGTCCAAGACTTTGG
ATTTTCATTGATGTGCTTCTGCTGAGCAAGGATGAAGATGGGAAGGCATTGTCAGATGAGGAT
ATAAGAGCAGAGGCTGACACCTTCATGTTTGGAGGCCATGACACCACGGCCAGTGCCCTCTC
CTGGGTCTGTACAACCTTGCGAGGCACCCAGAATACCAGGAGCGCTGCCGACAGGAGGTGC
AAGAGCTTCTGAAGGACCGGATCCTAAAGAGATTGAATGGGACGACCTGGCCCAGCTGCCC
TTCCTGACCATGTGCGTGAAGGAGAGCCTGAGGTTACATCCCCCAGCTCCCTTCATCTCCCG
ATGCTGCACCCAGGACATTGTTCTCCAGATGGCCGAGTCATCCCCAAAGGCATTACCTGCC
TCATCGATATTATAGGGGTCCATCACAACCCAACTGTGTGGCCGGATCCTGAGGTCTACGAC
CCCTTCCGCTTTGACCCAGAGAACAGCAAGGGGAGGTACCTCTGGCTTTTATTCTTTCTC
CGCAGGGCCCAGGAACTGCATCGGGCAGGCGTTTCGCCATGGCGGAGATGAAAGTGGTCCTGG
CGTTGATGCTGCTGCACCTTCCGGTTCCCTGCCAGACCACACTGAGCCCCGAGGAAGCTGGAA
TTGATCATGCGCGCCGAGGGCGGGCTTTGGCTGCGGGTGGAGCCCCGTAATGTAGGCTTGCA
GTGACTTTCTGACCCATCCACCTGTTTTTTTGCAGATTGTCATGAATAAAACGGTGCTGTCAAA

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FIGURE 182

MSLLSLPWLGLRPVAMSPWLLLLLVVGSWLLARILAWTYAFYNNCRRLQCFPPKRNWFWG
HLGLITPTEEGLKDSTQMSATYSQGFTVWLGPIIPFIVLCHPDTIRSITNASAAIAPKDNLF
IRFLKPWLGEKILLSGGDKWSRHRRLTPAFHFNILKSYITIFNKSANIMLDKWQHASEGS
SRLDMFEHISLMTLSLQKCIFSFDSHCQERPSEYIATILELSALVEKRSQHILQHMDFLYY
LSHDGRRFHRACRLVHDFDVAIRERRRRLTPTQGIDDFKDKAKSKTLDFFIDVLLLSKDEG
KALSDEDIRAEADTFMFGGHDTTASGLSWVLYNLARHPEYQERCQEVQELLKDRDPKEIEW
DDLAQLPFLTMCVKESLRLHPPAPFISRCCTQDIVLPDGRVIPKGITCLIDIIGVHHNPTVW
PDPEVYDPFRFDPENSKGRSPLAFIPFSAGPRNCIGQAFAMAEMKVVLALMLLHFRFLPDHT
EPRRKLELIMRAEGGLWLRVEPLNVGLQ

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FIGURE 183

CAACAGAAGCCAAGAAGGAAGCCGTCTATCTTGTGGCGATCATGTATAAGCTGGCCTCCTGC
TGTTTGCTTTTCACAGGATTCTTAAATCCTCTCTTATCTCTTCCTCTCCTTGACTCCAGGGA
AATATCCTTTCAACTCTCAGCACCTCATGAAGACGCGCGCTTAACTCCGGAGGAGCTAGAAA
GAGCTTCCCTTCTACAGATATTGCCAGAGATGCTGGGTGCAGAAAGAGGGGATATTCTCAGG
AAAGCAGACTCAAGTACCAACATTTTTTAACCCAAGAGGAAATTTGAGAAAGTTTCAGGATTT
CTCTGGACAAGATCCTAACATTTTACTGAGTCATCTTTTGGCCAGAATCTGGAAACCATACA
AGAAACGTGAGACTCCTGATTGCTTCTGGAAATACTGTGTCTGAAGTGAAATAAGCATCTGT
TAGTCAGCTCAGAAACACCCATCTTAGAATATGAAAAATAACACAATGCTTGATTTGAAAAC
AGTGTGGAGAAAAACTAGGCAAACTACACCCTGTTTCATTGTTACCTGGAAAATAAATCCTCT
ATGTTTTGCACAAAAAAAAAAAAAAAAA

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FIGURE 184

MYKLASCCLLFTGFLNPLLSLPLLDREISFQLSAPHEDARLTPEELERASLLQILPEMLGA
ERGDILRKADSSTNIFNPRGNLRKFQDFSGQDPNILLSHLLARIWKPYKKRETPDCFWKYCV

FIGURE 185

GAACATTTT TAGTTC CCAAGGAATGTACATCAGCCCCACGGAAGCTAGGCCACCTCTGGGAT
GGGGTTGCTGGTTTAAAACAAACGCCAGTCATCCTATATAAGGACCTGACAGCCACCAGGCA
CCACCTCCGCCAGGAAGTGCAGGCCCCACCTGTCTGCAACCCAGCTGAGGCCATGCCCTCCCC
AGGGACCGTCTGCAGCCTCCTGCTCCTCGGCATGCTCTGGCTGGACTTGGCCATGGCAGGCT
CCAGCTTCCTGAGCCCTGAACACCAGAGAGTCCAGCAGAGAAAGGAGTCAAGAAGCCACCA
GCCAAGCTGCAGCCCCGAGCTCTAGCAGGCTGGCTCCGCCCCGGAAGATGGAGGTCAAGCAGA
AGGGGCAGAGGATGAACTGGAAGTCCGGTTCAACGCCCCCTTTGATGTTGGAATCAAGCTGT
CAGGGGTT CAGTACCAGCAGCACAGCCAGGCCCTGGGGAAGTTTCTTCAGGACATCCTCTGG
GAAGAGGCCAAAGAGGCCCCAGCCGACAAGTGA TCGCCCCACAAGCCTTACTCACCTCTCTCT
AAGTTTAGAAGCGCTCATCTGGCTTTTCGCTTGCTTCTGCAGCAACTCCCACGACTGTTGTA
CAAGCTCAGGAGGCGAATAAATGTTCAAACCTGTA

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FIGURE 186

MPSPGTVCSLLLLGMLWLDLAMAGSSFLSPEHQRVQQRKESKKPPAKLQPRALAGWLRPEDG

GQAEGAEDELEVRFNAPFDVGIKLSGVQYQQHSQALGKFLQDILWEEAKEAPADKO

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FIGURE 187

CGGCCACAGCTGGCATGCTCTGCCTGATCGCCATCCTGCTGTATGTCCTCGTCCAGTACCTC
GTGAACCCCGGGGTGCTCCGCACGGACCCCAGATGTCAAGAATATGAACACGTGGCTGCTGT
TCCTCCCCCTGTTCCCGGTGCAGGTGCAGACCCTGATAGTCGTGATCATCGGGATGCTCGTG
CTCTGCTGGACTTTCTTGCTTGGTGCACCTGGGCCAGCTGCTCATCTTCCACATCTACCT
GAGTATGTCCCCACCCCTAAGCCCCCGATCCCCCAAGGCTGGGTGGTCAGAGCTGCTCATC
TTACACCTCTACTTGAGTATGTCCCTAACCCCTGAGCCCCCACGCCCTGGGGCCAGAGTCTTT
GTCCCCCGTGTGCGCATGTGTTTCAAGGTGAGCCTCTCCAGAAGTGAGATCATGGACAAAAA
GGGCAAATCACAGGAAGAAATTAAATCCATGAGGACCCAGCAGGCCCAAGAAGCTGAAC
TCACGCCGAGACCTGCAGGAGTGGTGCCAGGTGCTTGAAGTAACAAGTTTAAAAATGTTTCA
GACAATGGAATGGAATCTATTAGGCAAGAACAGGACATTATGAAATAAGGACAGGTGGACTT
CCAAAAACACAAGTAGAAATTCTAACAAATGAAATATATTACAGGCAGGTCACCCCTAACCA
AACAACTGAAGCGAGAGCTGTGGTCTTGCTTGGTCTCACAGTGGGCACAGCGGTAGGCGGTC
AGTCATGTTGCTGAACGACGGAGGGTAAACTCCCCAGCCCCAAGAAAACTGTGTTGGAAGT
AACAAACACCTCCCTGCTCCTGGCACCAGCCGTTTTTGGTCATGGTGGGCCAGCTGCAAAGCG
TCTTCCATTCTCTGGGCAGTGGTGGCCCCGAGGCTGTGGCCTCTCAGGGGGTTTCTGTGGAC
ACGGGCAGCAGAGTGTGTCCAGGCCAGCCCCCAAGAATGCCCTGCTCCTGACAGCTTGGCCA
ACCCCTGGTCAGGGCAGAGGGAGTTGGGTGGGTGAGGCTCTGGGCTCACCTCCATCTCCAGA
GCATCCCCTGCCTGCAGTTGTGGCAAGAACGCCAGCTCAGAATGAACACACCCCACCAAGA
GCCTCCTTGTTCATAACCACAGGTTACCCCTACAAACCACTGTCCCCACACAACCCCTGGGGAT
GTTTTTAAACACACACCTCTAACGCATATCTTACAGTCACTGTTGTCTTGCCTGAGGGTTGA
ATTTTTTTTAAATGAAAGTGCAATGAAAATCACTGGATTAAATCCTACGGACACAGAGCTGAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 188

MNTWLLFLPLFPVQVQTLIVVIIGMLVLLLDLGLVHLGQLLI FHIYLSMSPTLSPRSPQGW
VVRAAHLTPLLEYVPNPEPPTPGARVFVPRVRMCSGSASPRSEIMDKKGKSQEEIKSMRTQQ
AQQEAELTPRPAGVVPGA

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FIGURE 189

GGAGTGCAGATGGCATCCTTCGGTTCTTCCAGACAAAGCTGCAAGACGCTGACCAATGGCCAAG
ATGGAGCTCTCGAAGGCCTTCTCTGGCCAGCGGACACTCCTATCTGCCATCCTCAGCATGCT
ATCACTCAGCTTCTCCACAACATCCCTGCTCAGCAACTACTGGTTTGTGGGCACACAGAAGG
TGCCCCAAGCCCCCTGTGCGAGAAAAGGTCTGGCAGCCAAGTGCTTTGACATGCCAGTGTCCCTG
GATGGAGATACCAACACATCCACCCAGGAGGTGGTACAATACAACTGGGAGACTGGGGATGA
CCGGTTCTCCTTCCGGAGCTTCCGGAGTGGCATGTGGCTATCCTGTGAGGAACTGTGGAAG
AACCAGGGGAGAGGTGCCGAAGTTTCATTGAACTTACACCACCAGCCAAGAGAGGTGAGAAA
GGACTACTGGAATTTGCCACGTTGCAAGGCCCATGTCACCCCACTCTCCGATTTGGAGGGAA
GCGGTTGATGGAGAAGGCTTCCCTCCCCTCCCCTCCCCTTGGGGCTTTGTGGCAAAAATCCTA
TGGTTATCCCTGGGAACGCAGATCACCTACATCGGACTTCAATTCATCAGCTTCCTCCTGCT
ACTAACAGACTTGCTACTCACTGGGAACCCTGCCTGTGGGCTCAAACTGAGCGCCTTTGCTG
CTGTTTCTCTGTCTCTGTCTCAGGTCTCCTGGGGATGGTGGCCCCACATGATGTATTCAACAAGTC
TTCCAAGCGACTGTCAACTTGGGTCCAGAAGACTGGAGACCACATGTTTGGAATTATGGCTG
GGCCTTCTACATGGCCTGGCTCTCCTTCACCTGCTGCATGGCGTCGGCTGTCACCACCTTCA
ACACGTACACCAGGATGGTGCTGGAGTTCAAGTGCAAGCATAGTAAGAGCTTCAAGGAAAAC
CCGAACTGCCTACCACATCACCATCAGTGTTCCTCGGCGGCTGTCAAGTGACGCCCCAC
CGTGGGTCCTTTGACCAGCTACCACCAGTATCATAATCAGCCCATCCACTCTGTCTCTGAGG
GAGTCGACTTCTACTCCGAGCTGCGGAACAAGGGATTTCAAAGAGGGGCCAGCCAGGAGCTG
AAAGAAGCAGTTAGGTCATCTGTAGAGGAAGAGCAGTGTTAGGAGTTAAGCGGGTTTGGGGA
GTAGGCTTGAGCCCTACCTTACACGTCTGCTGATTATCAACATGTGCTTAAGCCAACATCCG
TCTCTTGAGCATGGTTTTTAGAGGCTACGAATAAGGCTATGAATAAGGGTTATCTTTAAGTC
CTAAGGGATTCTGGGTGCCACTGCTCTCTTTTCTCTACAGCTCCATCTGTTCACCCAC
CCCACATCTCACACATCCAGAATTCCTTCTTTACTGATAGTTTCTGTGCCAGGTCTGGGC
TAAACCATGGAGATAAAAAGAAGAGTAAATACACTTCCCGACCTTAAGGATCTGAAA

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FIGURE 190

MAKMELSKAFSGQRTLLSAILSMLSLSFSTTSLLSNYWFVGTQKVPKPLCEKGLAAKCFDMP
VSLDGD TNTSTQEVVQYNWETGDDRFSFRSFRSGMWLSCEETVEEPGERCRSFIELTPPAKR
GEKGLLEFATLQGPCHPTLRFGGKRLMEKASLPSPPLGLCGKNPMVIPGNADHLHRTSIHQL
PPATNRLATHWEPCLWAQTERLCCCFLCPVRSPGDGGPHDVFTSLPSDCQLGSRRLETTCL
LWLGLLHGLALLHLLHGVGCHHLQHVHQDGAGVQVQA

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FIGURE 191

AACTGGAAGGAAAGAAAGAAAGGTCAGCTTTGGCCCAGATGTGGTTACCCCTTGGTCTCCTG
TCTTTATGTCTTTCTCCTCTTCCTATTCTGTCATCTCCCTCACTTAAGTCTCAGGCCTGTCA
GCAGCTCCTGTGGACATTGCCATCCCCCTCTGGTAGCCTTCAGAGCAAAACAGGACAACCTATG
TTATGGATGTTTCCACCAACCAGGGTAGTGGCATGGAGCACCGTAACCATCTGTGCTTCTGT
GATCTCTATGACAGAGCCACTTCTCCACCTCTGAAATGTTCCCTGCTCTGAAATCTGGCATG
AGATGGCACAGGTGACCACGCAGAAGCCACCAGAATCTTGCCCTGCCCTATTCCCTCCTCCCAA
GTCTGTTCTCTTATTGTCAACCTCAGCACAAACAGGCTGGCGCCAATGGCATTACAGAGAAAG
CAATCTGTGTGGCTAGTGGGCAGATTACCATGCAAGCCCCAGGAGAAATGGAGGAGCTTTGT
AGCCACCTCCCTGTCAGCCAGTATTAACATGTCCCCCTCCCCCTGCCCCGCGTAGATTACAG
GACATTCGCCCCCTGTGTGCCACCAAACCAGGACTTTCCCCCTTGGCTTGGCATCCCTGGCTCT
CTCCTGGTACCCAGCAAGACGTCTGTTCCAGGGCAGTGTAGCATCTTTCAAGCTCCGTTACT
ATGGCGATGGCCATGATGTTACAATCCCCTTGCCTGAATAATCAAGTGGGAAGGGGAAGCA
GAGGGAAATGGGGCCATGTGAATGCAGCTGCTCTGTTCTCCCTACCCCTGAGGAAAAACCAA
GGGAAGCAACAGGAACTTCTGCAACTGGTTTTTATCGGAAAGATCATCCTGCCTGCAGATGC
TGTTGAAGGGGCACAAGAAATGTAGCTGGAGAAGATTGATGAAAGTGCAGGTGTGTAAGGAA
ATAGAACAGTCTGCTGGGAGTCAGACCTGGAATTCTGATTCCAAACTCTTTATTACTTTGGG
AAGTCACTCAGCCTCCCCGTAGCCATCTCCAGGGTGACGGAACCCAGTGTATTACCTGCTGG
AACCAAGGAAACTAACAATGTAGGTTACTAGTGAATACCCCAATGGTTTCTCCAATTATGCC
CATGCCACCAAAACAATAAAACAAAATTCTCTAACACTGAAA

FIGURE 192

MWLPLGLLSLCLSPLPILSSPSLKSQACQQLLWTLPSPLVAFRANRTTYVMDVSTNQSGME
HRNELCFCDLYDRATSPPLKCSLL

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FIGURE 193

GTAGCGCGTCTTGGGTCTCCCGGCTGCCGCTGCTGCCGCCGCCGCTCGGGTCGTGGAGCCA
GGAGCGACGTCACCGCCATGGCAGGCATCAAAGC'TTGATTAGTTTGTCTTTGGAGGAGCA
ATCGGACTGATGTTTTTGGATGCTTGGATGTGCCCTTCCAATATACAACAAATACTGGCCCT
CTTTGTTCTATTTTTTACATCCTTTACCTATTCCATACTGCATAGCAAGAAGATTAGTGG
ATGATACAGATGCTATGAGTAACGCTTGTAAGGAACCTGCCATCTTTCTTACAACGGGCATT
GTCGTGTGAGCTTTTGGACTCCCTATTGTATTGTCAGAGCACATCTGATTGAGTGGGGAGC
TTGTGCACTTGTCTCACAGGAAACACAGTCATCTTTGCAACTATACTAGGCTTTTTCTTGG
TCTTTGGAAGCAATGACGACTTCAGCTGGCAGCAGTGGTGAAGAAATTAAGAACTATTG
TCAAATGGACTTCCTGTCAATTTGTTGGCCATTACGCACACAGGAGATGGGGCAGTTAATGC
TGAATGGTATAGCAAGCCTCTTGGGGGTATTTTAGGTGCTCCCTTCTCACTTTTATTGTAAG
CATACTATTTTACAGAGACTTGCTGAAGGATTAAGGATTTTCTTTTTGGAAGCTTG
ACTGATTTTCACTTATCTATAGTATGCTTTTTTGTGGTGTCTGCTGAATTTAAATATTTAT
GTGTTTTTCTGTTAGGTGATTTTTTTTTGGAATCAATATGCAATGTTAAACACTTTTTTAA
TGTAATCATTTGCATTGGTTAGGAATTCAGAATTCGCCGGCTCTATTACTGGTCAAGTACA
TCTTTTCTCTTAAATATTTAGCCTCCATTATTACAAAAAATTATAAAAAATAAGTTTTCAG
TCAGTCAGGATGACATCACTCCCAATGTTATGCAGACATACAGACGGTTGGCATACTGTTATA
GACTGTATACTCAGTGCAAATATAGCTGCATTTATACCTCAGAGGGGCCAAGTGTTAATGCC
CATGCCCTCCGTTAAGGGTTGTTGGTTTTACTGGTAGACAGATGTTTTGTGGATTGAAAATT
ATTTTATGGAATTGCTACAGAGGAGTGCTTTTCTCTCAATTGTTAGAAGAATTTATGTTAA
ACTTTAAGGTAAGGGTGTAACAACTTTTTGAGATAAGGTTTTTATTTATGTTTATTATTGT
TAGAGTGAGTTGCAATGTGGGAAGAAATGACATTGAAATTCAGTTTTTGAATCCTGTTTCT
ATTTATAAGTGAAATTTGTGATCTCCTATCAACCTTTTATGTTTTACCCTGTTAAATGGAC
ATACATGGAACCACTACTGATGAGGGACAGTTGTATGTTGCATCATATATGCCAGAAAACC
TTCTCTGCTTCTCTCTTTTGAATTTTGGTATGTTGTATATATTACATAAAATAACTTTT
CAAATATAGTTTAAATAACACTTAGAAGTGTTTACTTACCTGGAAAATAATTGCTATGCCGTA
CATTACAGAGTGCCCCCTCCCCTGCAAGGCCTTGCCATGATTAACAAGTAACTTGTTAGTCTT
ACAGATAATTATGCATTAACAGTTTAAAGATTTAGACCATGGTAATAGTAGTTCCTTATTCTC
TAAGGTTATATCATATGTAATTTAAAGTATTTTAAAGACAAGTTTCTGTATACCTCTGAA
CTGTTTTGATTTTGAATTCATCATGATAGATCTGCTGTTTCTTATAAAAGGCATTTGTTGT
GTGAGTTAATGCAAAGTAGCCAAGTCCAGCTATATAGCAGCTTCAGAAACATACCTGACCAA
AAAATTTCCAGTAACCAAGGCATGATCAATTTATAGTGGTCGTTTACATCTAATAATTATCAG
GACTTTTTTTCAGGAGTGGGTATATAAAACATTCAAGTTGGTCTGACAGTATTTTGTAAAGGA
TATTTGTTTGTATGTTTATTCAGTATACTTACATAAAATTTATTTGCCATCAGCCAAAAC
CAGTAATCATGACAGCTGTCTGTTGTTTTATGAAGTTTATTTCTCAAGAAAATGGGAATAAA
TTTGGGATTTGTTGAGCTTTTTTACTAAAGATGCCTAAAGCCACAGGTTTTATTGCCAACT
TAAGCCATGACTTTTAGATATGAGATGACGGGAAGCAGGACGAAATATCGGCGTGTGGCTGG
AGCCTTCCCCTGAGGCTGAAAGTGGCTTGTGGTATTATAATGTTTCAAGAGGAA
GGTGCAGGTACACATGAGTTAGAGAGCTGGTGAGACAGTTGGGAACCTTTTGTGCTTGTGAT
CTACTGGACTTTTTTTTTGTCAGGAAGTGCAATTCCTGGTCCTTCCCTATTTTCTGTTCTGGA
TGTCAGTGACAGTGCACTGCTACTGTTTTATCCACTTGGCCACAGACTTTTTCTAACAGCTGC
GTATTATTTCTATATACTAATTGCATTGGCAGCATTGTGTCTTTGACCTTGTATACTAGCTT
GACATAGTGCTGTCTCTGATTTCTAGGCTAGTTACTTGAAGATATGAATTTTCCATAGAATAT
GCACTGATACAACATTACCATTCTTCTATGGAAAGAAAACCTTTGATGATGAAACAATAAAG
ATTTTAAATATCTATTTTAAAAAATAA

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FIGURE 194

MAGIKALISLSFGGAIGLMFLMLGCALPIYNKYWPLFVLFFYILSPIPYCIARRLVDDTDAM
SNACKELAIFLTGTGIVVSAFGLP1VFARAHLEWGACALVLTGNTVIFATILGFFLVFGSND
DFSWQQW

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FIGURE 195A

CCCACGCGTCCGCCCCACGCGTCCGCCCCACGCGTCCGCCCCACGCGTCCGCGC
 CACGCGTCCGCCCCACGCGTCCGGTGCAGCTCGCGCCGCACACTGCCTGGTGGAGGAAGGA
 GCCCGGGCGCCTCTCGCCGCTCCCCGCGCCCGCGTCCGCACCTCCCCACCGCCCGCCGCGC
 CCGCCCCGCGCCCGCAAAGCATGAGTGAGCCCGCTCTCTGCAGCTGCCCGGGGCGCGAATGG
 CAGGCTGTTTCCGCGGAGTAAAAGGTGGCGCCGTCAGTGGTCTTCCAATGACGGACATT
 AACCAGACTGTCAGATCCTGGGGAGTCGCGAGCCCCGAGTTTGGAGTTTTTCCCCCACAA
 CGTCACAGTCCGAACTGCAGAGGGAAGGAAGGCGGCAGGAAGGCGAAGCTCGGGCTCCGG
 ACGTAGTTGGGAAACTTGCGGTCCCTAGAACTCGCCTCCCCGCTTGGCGGGCCCTTGCA
 GCGCCGAGCCGAGCAGCAAAGTGAGACATTGTGCGCTGCCAGATCCGCGCGCCGCGGACCG
 GGGCTGCCTCGGAAACACAGAGGGTCTTCTCTCGCCCTGCATATAATTAGCCTGCACACAA
 AGGGAGCAGCTGAATGGAGGTTGTACTCTCTGGAAAAGGATTTCTGACCGAGCGCTTCCAA
 TGGACATTCTCCAGTCTCTCTGGAAAGATTCTCGTAATGGATTTCCTGCTGCTCGGTCTCT
 GTCTATAGTGGCTGCTGAGGAGGCCCTCGGGGGTGGTCTTGTGTCTGCTGGGGGCTGCTT
 CAGATGCTGCCCGCCGCCCCAGCGGTGCCCGCAGCTGTGCCGGTGCGAGGGGCGGCTGCT
 GTACTGCGAGGCGCTCAACCTCACCGAGGCGCCCCACAACCTGTCCGGCCTGCTGGGCTTGT
 CCCTGCGCTACAACAGCCTCTCGGAGCTGCGCGCCGGCCAGTTACGGGGTTAATGCAGCTC
 ACGTGGCTCTATCTGGATCAAACTCACATCTGCTCCGTGCAGGGGACGCCTTTCAGAAACT
 GCGCCGAGTTAAGGAACTCACGCTGAGTTCCAACAGATCACCCAACTGCCCAACACCACCT
 TCCGGCCCATGCCCAACCTGCGCAGCGTGGACCTCTCGTACAACAAGCTGCAGGCGCTCGCG
 CCGACCTCTTCCACGGGCTGCGGAAGCTCACCACGCTGCATATGCGGGCCAAACGCCATCCA
 GTTGTGCGCGTGCGCATCTTCCAGGACTGCCGAGCCTCAAGTTTCTCGACATCGGATACA
 ATCAGCTCAAGAGTCTGGCGCGCAACTCTTTCGCGCGCTTGTTTAAGCTCACCGAGCTCGAC
 CTCGAGCACAACGACTTGGTCAAGGTGAACTTCGCCCACTTCCCGCGCCTCATCTCCCTGCA
 CTCGCTCTGCCCTGCGGAGGAACAAGGTGGCCATTGTGGTCAGCTCGCTGGACTGGGTTTGGGA
 ACCTGGAGAAAATGGACTTGTGCGGCAACGAGATCGAGTACATGGAGCCCCATGTGTTGAG
 ACCGTGCCGCACCTGCAGTCCCTGCAGCTGGACTCCAACCGCCTCACCTACATCGAGCCCCG
 GATCCTCAACTCTTGGAAAGTCCCTGACAAGCATCACCTGCGCGGGAACCTGTGGGATTGCG
 GCGCAACGTGTGTGCCCTAGCCTCGTGGCTCAGCAACTTCAGGGGCGCTACGATGGCAAC
 TTGCAGTGCGCCAGCCCGAGTACGCACAGGGCGAGGACGCTCCTGGACGCCGTGTACGCCTT
 CCACCTGTGCGAGGATGGGGCCGAGCCACAGCGGCCACCTGCTCTCGGCCGTACCAACC
 GCAGTGATCTGGGGCCCCCTGCCAGCTCGGCCACACGCTCGCGGACGCGGGGAGGGGACG
 CACGACGGCACATTGAGCCTGCCACCGTGGCTCTTCCAGGCGGCGAGCACGCCGAGAACGC
 CGTGACAGATCCACAAGGTGGTCACGGGCACCATGGCCCTCATCTTCTCCTTCCTCATCGTGG
 TCCTGGTGTCTACGTGTCTGGAAGTGTTTCCAGCCAGCCTCAGGCAGCTCAGACAGTGC
 TTTGTACGCGAGCGCAGGAAGCAAAAGCAGAAACAGACCATGCATCAGATGGCTGCCATGTC
 TCCAGGATACTACGTTGATTACAAACCAGAACACATTGAGGGAGCCCTGGTGATCATCA
 ACGAGTATGGCTCGTGACCTGCCACCAGCAGCCCGCGAGGGAATGCGAGGTGTGATTGTCC
 CAGTGGCTCTCAACCCATGCGCTACCAAATACGCTGGGCAGCCGGGACGGGCCGCGGGCA
 CCAGGCTGGGGTCTCCTTGTCTGTGCTCTGATATGCTCCTTGACTGAAACTTTAAGGGGATC
 TCTCCAGAGACTTGACATTTTAGCTTTATTGTGTCTTAAAAACAAAAGCGAATTAAAAAC
 AACAAAAACCCCCACCCCAACCTTCAGGACAGTCTATCTTAAATTTTCATATGAGAACTCC
 TTCTCCCTTTGAAGATCTGTCCATATTAGGAATCTGAGAGTGTAAAAAAGGTGGCCATAA
 GACAGAGAGAGAAATAATCGTGCTTTGTTTATGCTACTCCTCCCACCTGCCCATGATTAAA
 CATCATGTATGTAGAAGATCTTAAGTCCATACGCATTTTCATGAAGAACCATTGGAAAGAGGA
 ATCTGCAATCTGGGAGCTTAAGAGCAATGATGACCATAGAAAGCTATGTTCTTACTTTGTG
 TGTGTGTCTGTATGTTTCTGCGTTGTGTGTCTTTGTAGGCAAGCAAACGTTGTCTACACAA
 CGGGAATTTAGCTCACATCATTTTCATGCCCTGTGCCTCTAGCTCTGGAGATTGGTGGGGG
 AGGTGGGGGGAACCGGCAGGAATAAGGGAAAGTGGTAGTTTTAACTAAGGTTTTGTAACT
 TGAAATCTTTTCTTCTCAAATTAATTATCTTTAAGCTTCAAGAACTTGCTCTGACCCCTC
 TAAGCAAACCTAAGCATTAAAAAGAGAATCTAATTTTTAAAGGTGTAGCACCTTTTTTTTT
 TATTCTTCCACAGAGGGTGCTAATCTCATTATGCTGTGCTATCTGAAAAGAACTTAAGGCC
 ACAATTCACGTCTCGTCTGGGCATTGTGATGGATTGACCTCCATTTGCAGTACCTTCCCA
 GCTGATTAAAGTTTCAGCAGTGGTATTGAGGTTTTTCGAATATTTATATAGAAAAAAGTCTT
 TTCACATGACAAATGACACTCTCACACCAGTCTTAGCCCTAGTAGTTTTTTAGGTTGGACCA
 GAGGAAGCAGGTTAAATGAGACCTGTCTCTGCTGCACTCAGAAAAAATAGGCAGTCCCTGA
 TGCTCAGATCTTAGCCTTGATATTAATAGTTGAGACCACCTACCCACAATGCAGCCTATACT
 CCCAAGACTACAAAGTTACCATCGCAAAGGAAAGGTTATTCCAGTAAAAGGAAATAGTTTTCT
 TCAACCATTTAAAAATATTCTTCTGAACCTCATCAAAGTAGAAGAGCCCCAACCTTTTCTCT
 CTGCCTTCAAGAAGGCAGACATTTGGTATGATTAGCATCAACAACACATTTATGAGTATAT

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FIGURE 195B

GTAAGTAATCAGAGGGGCAAATGCCACTTGTTATTCCTCCCAAGTTTTCCAAGCAAGTACAC
ACAGATCTCTGGTAGGATTAGGGGCCACTTGTTGTTTCCGGCTTATTTTAGTCGACTTGTGAG
CAAGTTTGATGCCTAGTCTATCTGACATGGCCCAGTAGAACAGGGCATTGATGGATCACATG
AGATGGTAGAAGGAACATCATCACATACCCCTCTCACAGAGAAAATTATCAAAGAACCAGAA
ATTATATCTGTTTTGGAGCAAGAGTGTGATAATGTTTCAGGGTAGTCAAAATAAACATAAAT
TATCTCCTCTAGATGAGTGGCGATGTTGGCTGATTTGGGTCTGCCATTGACAGAATGTCAAA
TAAAAAGGAATTAGCTAGAATATGACCATTAAATGTGCTTCTGAAATATATTTTGAGATAGG
TTTAGAATGTCA

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FIGURE 196

MDFLLLGLCLYWLLRRPSGVVLCLLGACFQMLPAAPSGCPQLCRCEGRLLYCEALNLTEAPH
NLSGLLGLSLRYNSLSELRAGQFTGLMQLTWLYLDHNIHICSVQGDAFQKLRRVKELTLSSNQ
ITQLPNTTFRPMPNLRSDLSYNKLQALAPDLFHGLRKLTTLHMRANAIQFVPVRIFQDCRS
LKFLDIGYNQLKSLARNSFAGLFKLTELHLEHNDLVKVNFAHFPRLISLHSLCLRRNKVAIV
VSSLDWVWNLEKMDLSGNEIEYMEPHVFETVPHLQSLQLDSNRLTYIEPRILNSWKSLSIT
LAGNLWDCGRNVCALASWLSNFQGRYDGNLQCASPEYAQGEDVLDVYAFHLCEDGAEPTSG
HLLSAVTNRSDLGPPASSATTADGGEGQHDGTFEPATVALPGGEHAENAVQIHKVVTGTMA
LIFSFLIVVLVLYVSWKCFPASLRQLRQCFVTQRRKQKQKQTMHQAAMSAQEYYVDYKPNH
IEGALVIINEYGSCTCHQQPARECEV

FIGURE 197

GTGCAAGGAGCCGAGGCGAGATGGGCGTCCTGGGCCGGGTCTGCTGTGGCTGCAGCTCTGC
GCACTGACCCAGGCGGTCTCCAACTCTGGGTCCCCAACACGGACTTCGACGTCGCAGCCAA
CTGGAGCCAGAACCGGACCCCGTGCGCCGGCGGCGCCGTTGAGTTCCCGGCGGACAAGATGG
TGTCAGTCCTGGTGCAAGAAGGTCACGCCGTCTCAGACATGCTCCTGCCGCTGGATGGGGAA
CTCGTCCTGGCTTCAGGAGCCGGATTGGGCGTCTCAGACGTGGGCTCGCACCTGGACTGTGG
CGCGGGCGAACCTGCCGTCTTCGCGACTCTGACCGCTTCTCCTGGCATGACCCGCACCTGT
GGCGCTCTGGGGACGAGGCACCTGGCCTCTTCTTCGTGGACGCCGAGCGCGTGCCCTGCCGC
CACGACGACGTCTTCTTTCCGCCTAGTGCCTCCTTCGCGTGGGGCTCGGCCCTGGCGCTAG
CCCCGTGCGTGTCCGCAGCATCTCGGCTCTGGGCCGGACGTTACGCGCGACGAGGACCTGG
CTGTTTTCTGGCGTCCCGCGCGGGCCGCCTACGCTTCCACGGGCCGGGCGCGCTGAGCGTG
GGCCCCGAGGACTGCGCGGACCCGTGGGCTGCGTCTGCGGCAACGCGGAGGCGCAGCCGTG
GATCTGCGCGGCCCTGCTCCAGCCCCCT

FIGURE 198

MGVLGRVLLWLQLCALTQAVSKLWVPNTDFDVAANWSQNRTPCAGGAVEFPADKMVSVLVQE
GHAUSDMLLPDGLVVLASGAGFGVSDVGSHLDCCGAGEPAVFRDSDRFSWHDPHLWRSIDEA
PGLFFVDAERVPCRHDDVFFPPSASFVGLGPGASPVVRVRSISALGRFTTRDEDLAVFLASR
AGRLRFHGFALSVGPEDCADPSGCVCGNAEAQPWICAALLQP

[illegible]

FIGURE 200

MGPVKQLKRMFEPTRLIATIMVLLCFALTLCSAFWWHNKGLALIFCILQSLALTWYSLSFIP
FARDAVKKCFVCLA

FIGURE 201

TTGAGCGCAGGTGAGCTCCTGCGCGTTCCGGGGGCGTTCTCCAGTCACCCTCCCGCCGTTA
CCCGCGGCGCGCCCGAGGGAGTCTCCTCCAGACCCTCCCTCCCGTTGCTCCAACTAATACG
GACTGAACGGATCGCTGCGAGGGTGGGAGAGAAAATTAGGGGGAGAAAGGACAGAGAGAGCA
ACTACCATCCATAGCCAGATAGATTATCTTACACTGAACTGATCAAGTACTTTGAAAATGAC
TTCGAAATTTATCTTGGTGTCTTCATACTTGCTGCACTGAGTCTTCAACCACCTTTTCTC
TCCAAC TAGACCAGCAAAAGGTTCTACTAGTTTCTTTTGATGGATTCCGTTGGGATTACTTA
TATAAAGTTCCAACGCCCCATTTTCATTATATTTATGAAATATGGTGTTACAGTGAAGCAAGT
TACTAATGTTTTATTACAAAACCTACCCTAACCATTTACTTTGGTAACTGGCCTCTTTG
CAGAGAATCATGGGATTGTTGCAAATGATATGTTTGATCCTATTTCGGAACAAATCTTTCTCC
TTGGATCACATGAATATTTATGATTCCAAGTTTTGGGAAGAAGCGACACCAATATGGATCAC
AAACCAGAGGGCAGGACATACTAGTGGTGCAGCCATGTGGCCCGGAACAGATGTAAAATAC
ATAAGCGCTTTCTACTCATTACATGCCTTACAATGAGTCAGTTTCATTTGAAGATAGAGTT
GCCAAAATGTTGAATGGTTTACGTCAAAGAGCCCATAAATCTTGGTCTTCTCTATTGGGA
AGACCCTGATGACATGGGCCACCATTGGGACCTGACAGTCCGCTCATGGGGCCTGTCATTT
CAGATATTGACAAGAAGTTAGGATATCTCATACAAATGCTGAAAAAGGCAAAGTTGTGGAAC
ACTCTGAACCTAATCATCACAAGTGATCATGGAATGACGCAGTGCTCTGAGGAAAGGTTAAT
AGAACTTGACCAGTACCTGGATAAAGACCACTATACCCTGATTGATCAATCTCCAGTAGCAG
CCATCTTGCCAAAAGAAGGTAAATTTGATGAAGTCTATGAAGCACTAACTCACGCTCATCCT
AATCTTACTGTTTACAAAAAAGAAGACGTTCCAGAAAGGTGGCATTACAAATACAACAGTCG
AATTCAACCAATCATAGCAGTGGCTGATGAAGGGTGGCACATTTTACAGAATAAGTCAGATG
ACTTTCTGTTAGGCAACCACGGTTACGATAATGCGTTAGCAGATATGCATCCAATAATTTTA
GCCCCATGGTCTGCTTCAGAAAGAAATTTCTCAAAGAGCCATGAACTCCACAGATTTGTA
CCCCTACTATGCCACCTCCTCAATATCACTGCCATGCCACACAATGGATCATTCTGGAATG
TCCAGGATCTGCTCAATTCAGCAATGCCAAGGGTGGTCCCTTATACACAGAGTACTATACTC
CTCCCTGGTAGTGTTAAACCAGCAGAATATGACCAAGAGGGGTCTATACCCTTATTTTCATAGG
GGTCTCTCTTGGCAGCATTATAGTGATTGTATTTTTTGTAATTTTCATTAAGCATTTAATTC
ACAGTCAAATACCTGCCTTACAAGATATGCATGCTGAAATAGCTCAACCATTATTACAAGCC
TAATGTTACTTTGAAGTGGATTTGCATATTGAAGTGGAGATTCCATAATTATGTCAGTGTTT
AAAGGTTTCAAATTTCTGGGAAACCAGTTCCAAACATCTGCAGAAACCATTAAAGCAGTTACAT
ATTTAGGTATACACACACACACACACACATACACACACACCGACCAAAATACTTACAC
CTGCAAAGGAATAAAGATGTGAGAGTATGTCTCCATTGTTCACTGTAGCATAGGGATAGATA
AGATCCTGCTTTATTTGGACTTGGCGCAGATAATGTATATATTTAGCAACTTTGCACTATGT
AAAGTACCTTATATATTGCATTTAAATTTCTCTCCTGATGGGTACTTTAATTTGAAATGCA
CTTTATGGACAGTTATGTCTTATAACTTGATTGAAAATGACAACTTTTTGCACCCATGTAC
AGAATACTTGTTACGCATTGTTCAAACCTGAAGGAAATTTCTAATAATCCCGAATAATGAACA
TAGAAATCTATCTCCATAAATTGAGAGAAGAAGAAGGTGATAAGTGTTGAAAATTTAAATGTG
ATAACCTTTGAACCTTGAAATTTTGAGATGTATTCCCAACAGCAGAATGCAACTGTGGGCAT
TTCTTGCTTATTTCTTTCCAGAGAACGTGGTTTTTCATTTATTTTTCCCTCAAAGAGAGTC
AAATACTGACAGATTCGTTCTAAATATATTGTTTCTGTCTATAAAATTTATTGTGATTTCTCTGA
TGAGTCATATTACTGTGATTTTCTAATAATGAAGACACCATGAATATACTTTTCTCTATA
TAGTTTCAGCAATGGCCTGAATAGAAGCAACCAGGCACCATCTCAGCAATGTTTTCTCTGTT
TGTAATTAATTTGCTCCTTTGAAAATTAATCACTATTAATTACATTAAAAATCAAATTGGAT
AAAAAAAAAAAAAAAAAAAA

FIGURE 202

MTSKFILVSFILAALSLSTTFSLQLDQQKVLLVSFDGFRWDYLYKVPTPHFHYIMKYGVHVK
QVTNVFITKTYPNHYTLVTGLFAENHGIVANDMFDPIRNKSFSLDHMNIYDSKFWEETPIW
ITNQRAGHTSGAAMWPGTDVKIHKRFPTHYMPYNESVSFEDRVAKIVEWFTSKEPINLGLLY
WEDPDDMGHHLGPDSPLMGPVISDIDKKLGYLIQMLKKAKLWNTLNLIITSDHGMTQCSEER
LIELDQYLDKDHYYTLIDQSPVAAILPKEGKFDEVYEALTHAHPNLTVYKKEDVPERWHYKYN
SRIQPIIAVADEGWHILQNKSDDFLLGNHGYDNALADMHPIFLAHGPAFRKNFSKEAMNSTD
LYPLLCHLLNITAMPHNGSFWNVQDLLNSAMPRVVPYTQSTILLPGSVKPAEYDQEGSYPYF
IGVSLGSIIVIVFFVIFIKHLIHSQIPALQDMHAEIAQPLLQA

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FIGURE 203

GGATTTTTGTGATCCGCGATTGCTCCCACGGGCGGGACCTTTGTAAGTGCAGGAGGCCCAG
GACAGGCCCCACCCTGCGGGGCGGGAGGCAGCCGGGGTGAGGGAGGTGAAGAAACCAAGACGC
AGAGAGGCCAAGCCCCCTTGCTTGGGTACACAGCCAAAGGAGGCAGAGCCAGAACTCACAA
CCAGATCCAGAGGCAACAGGGACATGGCCACCTGGGACGAAAAGGCAGTCACCCGCAGGGCC
AAGGTGGCTCCCGCTGAGAGGATGAGCAAGTTCTTAAGGCACTTCACGGTCGTGGGAGACGA
CTACCATGCCTGGAACATCAACTACAAGAAATGGGAGAATGAAGAGGAGGAGGAGGAGG
AGCAGCCACCAACCACACCAGTCTCAGGCGAGGAAGGCAGAGCTGCAGCCCCCTGACGTTGCC
CCTGCCCCCTGGCCCCGCACCCAGGGCCCCCCTTGACTTCAGGGGCATGTTGAGGAACTGTT
CAGCTCCACAGGTTTCAGGTCATCATCATCTGCTTGGTGGTTCTGGATGCCCTCCTGGTGC
TTGCTGAGCTCATCCTGGACCTGAAGATCATCCAGCCCGACAAGAATAACTATGCTGCCATG
GTATTCACCTACATGAGCATCACCATCTTGGTCTTTTTTATGATGGAGATCATCTTTAAATT
ATTTGTCTTCCGCCTGAGTTCTTTCACCACAAGTTTGAGATCCTGGATGCCCGTCGTGGTGG
TGGTCTCATTCATCCTGGACATTGTCTCCTGTTCCAGGAGCACCAGTTTGAGGCTCTGGGC
CTGCTGATTCTGCTCCGGCTGTGGCGGGTGGCCCGGATCATCAATGGGATTATCATCTCAGT
TAAGACACGTTCAGAACGGCAACTCTTAAGGTTAAACAGATGAATGTACAATTGGCCGCCA
AGATTCAACACCTTGAGTTCAGCTGCTCTGAGAAGCCCCCTGGACTGATGAGTTTGCTGTATC
AACCTGTAAGGAGAAGCTCTCTCCGGATGGCTATGGGAATGAAAGAATCCGACTTCTACTCT
CACACAGCCACCGTGAAAGTCCTGGAGTAAATGTGCTGTGTACAGAAGAGAGAGAAGGAAG
CAGGCTGGCATGTTCACTGGGCTGGTGTACGACAGAGAACCTGACAGTCACTGGCCAGTTA
TCACTTCAGATTACAAATCACACAGAGCATCTGCCTGTTTTCAATCACAGAGAACAAAACC
AAAATCTATAAAGATATTCTGAAAATATGACAGAATTTGACAAATAAAAGCATAAACGTGTA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 204

MATWDEKAVTRRAKVAPAERMSKFLRHFTVVGDDYHAWNINYYKKWENEEEEEEQPPPTPV
SGEEGRAAAPDVAPAPGPAPRAPLDFRGLRKLFSSHRFQVIIICLVVLDALLVLAELIDL
KIIQPDKNYYAAMVFHYMSITILVFFMMEIIFKLFVFRLLSSFTTSLRSWMPVVVVVSFILD
VLLFQEHQFEALGLLILLRLWRVARIINGIIISVKTRSERQLRLKQMNVLAAKIQHLEFS
CSEKPLD

FIGURE 205

CGGCTCGAGCTCGAGCCGAATCGGCTCGAGGGGCGAGTGGAGCACCCAGCAGGCGGCCAACAT
 GCTCTGTCTGTGCCTGTACGTGC TGGTCATCGGGGAAGCCAGACCGAGTTCCAGTACTTTG
 AGTCGAAGGGGCTCCCTGCCGAGCTGAAGTCCATTTTCAAGCTCAGTGTCTTCATCCCCCTCC
 CAGGAATTCTCCACCTACCGCCAGTGGGAAGCAGAAAATTGTACAAGCTGGAGATAAGGACCT
 TGATGGGCGAGCTAGACTTTGAAGAATTTGTCCATTATCTCCAAGATCATGAGAAGAAGCTGA
 GGCTGGTGTTTAAGATTTTGGACAAAAAGAATGATGGACGCATTGACGCGCAGGAGATCATG
 CAGTCCCTGCGGGGACTTGGGAGTCAAGATATCTGAACAGCAGGCAGAAAAAATTCTCAAGAG
 CATGGATAAAAAACGGCACGATGACCATCGACTGGAACGAGTGGAGAGACTACCACCTCCTCC
 ACCCCGTGGAAAAACATCCCCGAGATCATCCTCTACTGGAAGCATTCCACGATCTTTGATGTG
 GGTGAGAATCTAACGGTCCCGGATGAGTTCACAGTGGAGGAGAGGCAGACGGGGATGTGGTG
 GAGACACCTGGTGGCAGGAGGTGGGGCAGGGGCCGTATCCAGAACCTGCACGGCCCCCCTGG
 ACAGGCTCAAGGTGCTCATGCAGGTCCATGCCTCCCGCAGCAACAACATGGGCATCGTTGGT
 GGCTTCACTCAGATGATTCGAGAAGGAGGGGCCAGGTCACTCTGGCGGGCAATGGCATCAAG
 CGTCCCTCAAAATTGCCCCCGAATCAGCCATCAAATTCTGGCCTATGAGCAGATCAAGCGCC
 TTGTTGGTAGTGACCAGGAGACTCTGAGGATTACGAGAGGCTTGTGGCAGGGTCTTGGCA
 GGGGCCATCGCCAGAGCAGCATCTACCCAATGGAGGTCTGAAGACCCGGATGGCGCTGCG
 GAAGACAGGCCAGTACTCAGGAATGCTGGACTGCGCCAGGAGGATCCTGGCCAGAGAGGGGG
 TGGCCGCTTCTACAAAGGCTATGTCCCCAACATGCTGGGCATCATCCCTATGCCCGCATC
 GACCTTGCAGTCTACGAGACGCTCAAGAATGCCTGGCTGCAGCACTATGCAGTGAACAGCGC
 GGACCCCGCGTGTGTTGTCTCCTGGCCTGTGGCACCATGTCCAGTACCTGTGGCCAGCTGG
 CCAGCTACCCCTGGCCCTAGTCAGGACCCGGATGCAGGCGCAAGCCTCTATTGAGGGCGCT
 CCGAGGTTGACCATGAGCAGCCTCTTCAAACATATCCTGCGGACCGAGGGGGCTTCGGGCT
 GTACAGGGGGCTGGCCCCCAACTTCATGAAGGTCAATCCAGCTGTGAGCATCAGCTACGTGG
 TCTACGAGAACCTGAAGATCACCTGGGCGTGCAGTTCGCGGTGA CGGGGGGAGGGCCGCCCCG
 GCAGTGGACTCGCTGATCCTGGGCCGAGCCTGGGGTGTGCAGCCATCTCATTCTGTGAATG
 TGCCAACACTAAGCTGTCTCGAGCCAAGCTGTGAAAACCTAGACGCACCCGAGGGAGGGT
 GGGGAGAGCTGGCAGGCCCAGGGCTTGTCTGTGCTGACCCAGCAGACCCTCCTGTTGGTTCC
 AGCGAAGACCACAGGCATTCTTAGGGTCCAGGGTCAGCAGGCTCCGGGCTCACATGTGTAA
 GGACAGGACATTTTCTGCAGTGCCTGCCAATAGTGAGCTTGGAGCCTGGAGGCCGGCTTAGT
 TCTTCCATTTTACCCTTGCAGCCAGCTGTTGGCCACGGCCCTGCCCTCTGGTCTGCCGTGC
 ATCTCCCTGTGCCCTCTTGCTGCCTGCCTGTCTGCTGAGGTAAGGTGGGAGGAGGGCTACAG
 CCCACATCCCACCCCTCGTCCAATCCCATAATCATGATGAAAGGTGAGGTCACTGGCCT
 CCCAGGCTGACTTCCCAACCTACAGCATTGACGCCAACTTGGCTGTGAAGGAAGAGGAAAG
 GATCTGGCCTTGTGGTCACTGGCATCTGAGCCCTGCTGATGGCTGGGGCTCTCGGGCATGCT
 TGGGAGTGCAGGGGGCTCGGGCTGCCTGGCCTGGCTGCACAGAAGGCAAGTGCTGGGGCTCA
 TGGTGTCTGAGCTGGCCTGGACCCTGTGAGGATGGGCCCCACCTCAGAACCAAACCTCACTG
 TCCCCACTGTGGCATGAGGGCAGTGGAGCACCATGTTTGGAGGCGAAGGGCAGAGCGTTTGT
 GTGTTCTGGGGAGGGAAGGAAAAGGTGTTGGAGGCCTTAATTATGGAAGTGTGGGAAAAGGG
 TTTTGTCCAGAAGGACAAGCCGGACAAATGAGCGACTTCTGTGCTTCCAGAGGAAGACGAGG
 GAGCAGGAGCTTGGCTGACTGCTCAGAGTCTGTTCTGACGCCCTGGGGGTTTCTGTCCAACC
 CCAGCAGGGGCGCAGCGGGACCAGCCCCACATTCCACTTGTGTCACTGCTTGGAACTTATT
 ATTTTGTATTTATTTGAACAGAGTTATGTCTCAACTATTTTATAGATTTGTTTAATTAATA
 GCTTGTCATTTTCAAGTTCATTTTTTATTTCATATTTATGTTTCATGGTTGATTGTACCTTCCC
 AAGCCCCCGCCAGTGGGATGGGAGGAGGAGGAGAAGGGGGGCTTGGGCCGCTGCAGTCACAT
 CTGTCCAGAGAAATTCCTTTTGGGACTGGAGGCAGAAAAGCGGCCAGAAGGCAGCAGCCCTG
 GCTCCTTTCTTTTGGCAGGTGGGGGAAGGGCTTGGCCCCAGCCTTAGGATTTAGGGTTTGA
 CTGGGGGCGTGGAGAGAGAGGGAGGAACCTCAATAACCTTGAAGGTGGAATCCAGTTATTTT
 CTGCGCTGCGAGGGTTTCTTTATTTCACTCTTTTCTGAATGTCAAGGCAGTGAGGTGCCTCT
 CACTGTGAATTTGTGGTGGGCGGGGGCTGGAGGAGAGGGTGGGGGGCTGGCTCCGTCCCTCC
 CAGCCTTCTGCTGCCCTTGCTTAACAATGCCGGCCAACCTGGCGACCTCACGGTTGCACTTCC
 ATTCACCAAGATGACCTGATGAGGAAATCTCAATAGGATGCAAGATCAATGCAAAAATT
 GTTATATATGAACATATAACTGGAGTCGTCAAAAAGCAAATTAAGAAAGAATTGGACGTTAG
 AAGTTGTCAATTAAGCAGCCTTCTAATAAAGTTGTTTCAAAGCTGAAAAAAAAAAAAAAAAA
 AA

FIGURE 206

MLCLCLYVPVIGEAQTEFQYFESKGLPAELKSIFKLSVFIPSQEFSTYRQWKQKIVQAGDKD
LDGQLDFEEFVHYLQDHEKKLRLVFKILDKKNDGRIDAQEQIMQSLRDLGVKISEQQAEEKILK
SMDKNGTMTIDWNEWRDYHLLHPVENIPEIILYWKHSTIFDVGENLTPDEFTVEERQTGMW
WRHLVAGGGAGAVSRTCTAPLDRCLKVLMQVHASRSNNMGIVGGFTQMIREGGARSLWRGNGI
NVLKIAPESAIKFMAYEQIKRLVGSDQETLRIHERLVAGSLAGAIQSSIYPMEVLKTRMAL
RKTGQYSGMLDCARRILAREGVAAFYKGYVPNMLGIIPYAGIDLAVYETLKNAWLQHYAVNS
ADPGVVFLLACGTMSSTCGQLASYPLALVRTRMQAQASIEGAPEVTMSSLFKHILRTEGAFG
LYRGLAPNFMKVIPAVSISYVVYENLKITLGVQSR

[illegible]

FIGURE 208

MASLGQILFWSIISIIIIILAGAIALIIGFGISGRHSITVTTVASAGNIGEDGILSCTFEPDI
KLSDIVIQWLKEGVLGLVHEFKEGKDELSEQDEMFRGRTAVFADQVIVGNASLRLKNVQLTD
AGTYKCYIITSKGKGNANLEYKTGAFSMPEVNVVDYNASSETLRCEAPRWFPPQPTVVWASQVD
QGANFSEVSNTSFELNSENVTMKVSVLYNVTINNTYSCMIENDIAKATGDIKVTETSEIKRR
SHLQLLNSKASLCVSSFFAISWALLPLSPYMLK

FIGURE 209

[illegible]

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FIGURE 210

MAASLGQVLALVLVAALWGGTQPLLKRASAGLQRVHEPTWAQQLQEMKTLFLNTEYLMPFL
LNQCGSLLYYLTLASTDLTLAVPICNSLAIFTLIVGKALGEDIGGKRKLDYCECGTQLCGS
RHTCVSSFPEPISPEWVRTRPFPILPFPLQLFCFLVAIRVPFPWTVWRKTEAGVWD

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FIGURE 211

CTTCTGTAGGACAGTCACCAGGCCAGATCCAGAAGCCTCTCTAGGCTCCAGCTTTCTCTGTG
GAAGATGACAGCAATTATAGCAGGACCTTGCCAGGCTGTCGAAAAGATTCCGCAATAAACT
TTGCCAGTGGGAAGTACCTAGTGAAACGGCCTAAGATGCCACTTCTTCTCATGTCCCAGGCT
TGAGGCCCTGTGGTCCCCATCCTTGGGAGAAGTCAGCTCCAGCACCATGAAGGGCATCCTCG
TTGCTGGTATCACTGCAGTGCTTGTTCAGCTGTAGAATCTCTGAGCTGCGTGCAGTGTAAT
TCATGGGAAAAATCCTGTGTCAACAGCATTGCCCTCTGAATGTCCCTCACATGCCAACACCAG
CTGTATCAGCTCCTCAGCCAGCTCCTCTCTAGAGACACCAGTCAGATTATACCAGAATATGT
TCTGCTCAGCGGAGAACTGCAGTGAGGAGACACACATTACAGCCTTCACTGTCCACGTGTCT
GCTGAAGAACACTTTTCATTTTGTAAGCCAGTGCTGCCAAGGAAAGGAATGCAGCAACACCAG
CGATGCCCTGGACCCCTCCCCTGAAGAACGTGTCCAGCAACGCAGAGTGCCCTGCTTGTTATG
AATCTAATGGAACCTTCCTGTCTGGGAAGCCCTGGAAATGCTATGAAGAAGAACAGTGTGTC
TTTCTAGTTGCAGAACTTAAGAATGACATTGAGTCTAAGAGTCTCGTGCTGAAAGGCTGTTT
CAACGTCAGTAACGCCACCTGTCACTTCCTGTCTGGTGAAAACAAGACTCTTGGAGGAGTCA
TCTTTTCGAAAGTTTGAGTGTGCAAATGTAAACAGCTTAACCCCCACGTCTGCACCAACCACT
TCCCACAACGTGGGCTCCAAAGCTTCCCTCTACCTCTTGGCCCTTGCCAGCCTCCTTCTTCG
GGGACTGCTGCCCTTGAGGTCCTGGGGCTGCACCTTTGCCCAGCACCCCATTTCTGCTTCTCTG
AGGTCCAGAGCACCCCTGCGGTGCTGACACCCTCTTCCCTGCTCTGCCCCGTTTAACTGC
CCAGTAAGTGGGAGTCACAGGTCTCCAGGCAATGCCGACAGCTGCCTTGTTCTTCATTATTA
AAGCACTGGTTTCATTCACTGCCAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 212

MKGILVAGITAVLVAAVESLSCVQCNSWEKSCVNSIASECPSHANTSCISSSASSSLETPVR
LYQNMFCSAENCSEETHITAFTVHVSAEEHFHFVSQCCQGKECSNTSDALDPPLKNVSSNAE
CPACYESNGTSCRGKPWKCYEEEQCVFLVAELKNDIESKSLVLKGCSNVSNATCQFLSGENK
TLGGVIFRKFECANVNSLTPTSAPTTSNHNVGSKASLYLLALASLLLRGLLP

FIGURE 213

GGCCTCGGTTCAAACGACCCGGTGGGTCTACAGCGGAAGGGAGGGAGCGAAGGTAGGAGGCA
GGGCTTGCCTCACTGGCCACCCTCCCAACCCCAAGAGCCCAGCCCCAATGGTCCCCGCCGCCG
GCGCGCTGCTGTGGGTCTGCTGCTGAATCTGGGTCCCCGGGCGGCGGGGGCCCAAGGCCTG
ACCCAGACTCCGACCGAAATGCAGCGGGTCAGTTTACGCTTTGGGGGCCCCATGACCCGCAG
CTACCGGAGCACCGCCCGGACTGGTCTTCCCCGGAAGACAAGGATAATCCTAGAGGACGAGA
ATGATGCCATGGCCGACGCCGACCGCCTGGCTGGACCAGCGGCTGCCGAGCTCTTGCCGCC
ACGGTGTCCACCGGCTTTAGCCGGTCGTCCGCCATTAACGAGGAGGATGGGTCTTCAGAAGA
GGGGGTTGTGATTAATGCCGGAAGGATAGCACAGCAGAGAGCTTCCAGTGCGACTCCCA
ATACAGCGGGAGTTCCAGCACGAGGTTTATAGCCAATAGTCAGGAGCCTGAAATCAGGCTG
ACTTCAAGCCTGCCGCGCTCCCCGGGAGGTCTACTGAGGACCTGCCAGGCTCGCAGGCCAC
CCTGAGCCAGTGGTCCACACCTGGGTCTACCCGAGCCGGTGGCCGTACCCCTCACCCACAG
CCATGCCATCTCCTGAGGATCTGCGGCTGGTGCTGATGCCCTGGGGCCCGTGGCACTGCCAC
TGCAAGTCGGGCACCATGAGCCGGAGCCGGTCTGGGAAGCTGCACGGCCTTTCCGGGCGCCT
TCGAGTTGGGGCGCTGAGCCAGCTCCGCACGGAGCACAAGCCTTGACCTATCAACAATGTC
CCTGCAACCGACTTCGGGAAGAGTGCCCCCTGGACACAAGTCTCTGTACTGACACCAACTGT
GCCTCTCAGAGCACCAACAGTACCAGGACCACCACTACCCCTTCCCCACCATCCACCTCAG
AAGCAGTCCCAGCCTGCCACCCGCCAGCCCCTGCCAGCCCTGGCTTTTGGAAACGGGTCA
GGATTGGCCTGGAGGATATTTGGAATAGCCTCTCTTCAGTGTTACAGAGATGCAACCAATA
GACAGAAACCAGAGGTAATGGCCACTTCATCCACATGAGGAGATGTCAGTATCTCAACCTCT
CTTGCCCTTTCAATCCTAGCACCCACTAGATATTTTTAGTACAGAAAAACAAACTGGAAAA
CACAA

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FIGURE 214

MVPAAGALLWVLLLNIGPRAAGAQGLTQTPTEMQRVSLRFGGPMTRSYRSTARTGLPRKTRI
ILEDENDAMADADRLAGPAAAEELLAATVSTGFSRSSAINEEDEDGSSEEGVVINAGKDSTSREL
PSATPNTAGSSSTRFIANSQEPEIRLTSSLPRSPGRSTEDLPGSQATLSQWSTPGSTPSRWF
SPSPTAMPSPEDLRLVLMWPWGPWHCHCKSGTMSRSRSGKLHGLSGRLRVGALSQLRTEHKPC
TYQQCPCNRLREECPLDTSLCDTNCASQSTTSTRTTTTPFPTIHLRSSPSLPPASPCPALA
FWKRVIRIGLEDIWNLSLSSVFTEMQPIDRNQR

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FIGURE 215

CCCCGGTTCGACCCACGCGTCCGGGGAGAAAGGATGGCCGGCCTGGCGGCGCGGTGGTCTCTG
CTAGCTGGGGCAGCGGCGCTGGCGAGCGGCTCCCAGGGCGACCGTGAGCCGGTGTACCGCGA
CTGCGTACTGCAGTGCAGAGCAGAACTGCTCTGGGGGCGCTCTGAATCACTTCCGCTCCC
GCCAGCCAATCTACATGAGTCTAGCAGGCTGGACCTGTGGGACGACTGTAAGTATGAGTGT
ATGTGGGTACCGTTGGGCTCTACCTCCAGGAAGGTCAAAAAGTGCCTCAGTTCCATGGCAA
GTGGCCCTTCTCCCGTTCTGTCTTTCAAGAGCCGGCATCGGCCGTGGCCTCGTTTCTCA
ATGGCCTGGCCAGCCTGGTGATGCTCTGCCGCTACCGCACCTTCGTGCCAGCCTCCTCCCC
ATGTACCACACCTGTGTGGCCTTCGCCTGGGTGTCCCTCAATGCATGGTTCTGGTCCACAGT
CTTCCACACCAGGGACACTGACCTCACAGAGAAAATGGACTACTTCTGTGCCTCCACTGTCA
TCCTACACTCAATCTACCTGTGCTGCGTCAGGACCGTGGGGCTGCAGCACCCAGCTGTGGTC
AGTGCCTTCCGGGCTCTCCTGCTGCTCATGCTGACCGTGACGTCTCCTACCTGAGCCTCAT
CCGCTTCGACTATGGCTACAACCTGGTGGCCAACGTGGCTATTGGCCTGGTCAACGTGGTGT
GGTGGCTGGCCTGGTGCTGTGGAACCAGCGGCGGTGCCTCACGTGCGCAAGTGCGTGGTG
GTGGTCTTGCTGCTGCAGGGGCTGTCCCTGCTCGAGCTGCTTGACTTCCACCGCTCTTCTG
GGTCTGGATGCCCATGCCATCTGGCACATCAGCACCATCCCTGTCCACGTCTCTTTTCA
GCTTCTGGAAGATGACAGCCTGTACCTGCTGAAGGAATCAGAGGACAAGTTCAAGCTGGAC
TGAAGACCTTGAGCGAGTCTGCCCCAGTGGGGATCCTGCCCCGCGCCTGCTGGCCTCCCTT
CTCCCCCTCAACCTTGAGATGATTTTCTCTTTTCAACTTCTTGAATTGGACATGAAGGATG
TGGGCCCAGAATCATGTGGCCAGCCACCCCTGTTGGCCCTCACCAGCCTTGAGTCTGTT
CTAGGGAAGGCCTCCAGCATCTGGGACTCGAGAGTGGGAGCCCTCTACCTCCTGGAGCT
GAACTGGGGTGGAACTGAGTGTGTTCTTAGCTCTACCGGAGGACAGCTGCCTGTTTCTCTCC
CCACCAGCCTCCTCCCCACATCCCCAGCTGCCTGGCTGGGTCTGAAGCCCTCTGTCTACCT
GGGAGACCAGGGACCACAGGCCTTAGGGATACAGGGGGTCCCCCTCTGTTTACACCCCCAC
CCTCCTCCAGGACACCACTAGGTGGTGTGATGCTTGTCTTTGGCCAGCCAAGGTTACG
GCGATTCTCCCATGGGATCTTGAGGGACCAAGCTGCTGGGATTGGGAAGGAGTTTACCCT
GACCGTTGCCCTAGCCAGGTTCCAGGAGGCCTCACCATACTCCCTTTCAGGGCCAGGGCTC
CAGCAAGCCAGGGCAAGGATCCTGTGCTGCTGTCTGGTTGAGAGCCTGCCACCGTGTGTG
GGAGTGTGGGCCAGGCTGAGTGCTAGGTGACAGGGCCGTGAGCATGGGCCTGGGTGTGTG
GAGCTCAGGCCTAGGTGCGCAGTGTGGAGACGGGTGTTGTGCGGGAAGAGGTGTGGCTTCAA
AGTGTGTGTGTGCAGGGGGTGGGTGTGTAGCGTGGGTAGGGGAACGTGTGTGCGCGTGT
GGTGGGCATGTGAGATGAGTGACTGCCGCTGAATGTGTCCACAGTTGAGAGGTTGGAGCAGG
ATGAGGGAATCCTGTCACCATCAATAATCACTTGTGGAGCGCCAGCTCTGCCCAAGACGCCA
CCTGGGCGGACAGCCAGGAGCTCTCCATGGCCAGGCTGCCTGTGTGCATGTTCCCTGTCTGG
TGCCCCCTTTGCGCGCTCCTGCAAACTCACAGGGTCCCCACACAACAGTGCCCTCCAGAAG
CAGCCCCCTCGGAGGCAGAGGAAGGAAAATGGGGATGGCTGGGGCTCTCTCCATCCTCCTTTT
CTCCTTGCCCTTCGCATGGCTGGCCTTCCCTTCCAAACCTCCATTCCCCCTGCTGCCAGCCCC
TTTGCCATAGCCTGATTTTGGGGAGGAGGAAGGGGCGATTTGAGGGAGAAGGGGAGAAAAGCT
TATGGCTGGGTCTGGTTTCTTCCCTTCCCAGAGGGTCTTACTGTTCCAGGGTGGCCCCAGGG
CAGGCAGGGGCCACACTATGCCTGTGCCCTGGTAAAGGTGACCCCTGCCATTTACCAGCAGC
CCTGGCATGTTCTGCCCCACAGGAATAGAATGGAGGGAGCTCCAGAACTTTCCATCCCAA
AGGCAGTCTCCGTGGTTGAAGCAGACTGGATTTTTGCTCTGCCCTGACCCCTGTCCCTCT
TTGAGGGAGGGGAGCTATGCTAGGACTCCAACCTCAGGGACTCGGGTGGCCTGCGTAGCTT
CTTTTGATACTGAAAACCTTTTAAGGTGGGAGGGTGGCAAGGGATGTGCTTAATAAATCAATT
CCAAGCCTCAAAAAAAAAAAAAAAAAA

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FIGURE 216

MAGLAARLVLLAGAAALASGSQGDREPVYRDCVLQCEEQNCSGGALNHFRSRQPIYMFLAGW
TCRDDCKYECMWVTVGLYLQEGHKVPQFHGKWPFSSRFLFFQEPASAVASFLNGLASLVMLCR
YRTFVPASSPMYHTCVAFWVSLNAFWSTVFHTRDTDLTEKMDYFCASTVILHSIYLCCVR
TVGLQHPAVVSAFRALLLMLTVHVSYSLSLIRFDYGYNLVANVAIGLVNVVWWLAWCLWNQR
RLPHVRKCVVVVLLQGLSLELLDFPPLFWVLDAAHAIWHISTIPVHVLFFSFLEDDSLYLL
KESEDKFKLD

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FIGURE 217

[illegible]

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FIGURE 218

MAPQSLPSSRMAPLGMLLGLLMAACFTFCLSHQNLKEFALTNPEKSSTKETERKETKAEEEL
DAEVLEVFPHTHEWQALQPGQAVPAGSHVRLNLQTGEREAKLQYEDKFRNNLK GKRLDINTN
TYTSQDLKSALAKFKEGAEMESSKEDKARQAEVKRLFRPIEELKKDFDELNVVIETDMQIMV
RLINKFNSSSSSLEEKIAALFDLEYYVHQMDNAQDLLSF GGLQVVINGLNSTEPLVKEYAAF
VLGAAFSSNPKVQVEAIEGGALQKLLVILATEQPLTAKKKVLFALCSLLRHFPYAQRQFLKL
GGLQVLR TLVQEKGTEVLAVRVVTLLYDLVTEKMF AEEEEAE LTQEMSPEKLQQYRQVHLLPG
LWEQGWCEITAHLLALPEHDAREKVLQTLGVLLTTCRDRYRQDPQLGRTLASLQAEYQVLAS
LELQDGEDEGYFQELLGSVNSLLKELR

TTCCGGCTTCCGTAGAGGAAGTGGCGCGGACCTTCATTTGGGGTTTCGGTTCCCCCTTCC
CTTCCCCGGGGTCTGGGGGTGACATTGCACCGCGCCCTCGTGGGGTCGCGTTGCCACCCCA
CGCGGACTCCCCAGCTGGCGCGCCCTCCCATTTGCCTGTCTGGTCAAGCCCCCACCCCC
TTCCCACCTGACCAGCAATGGGGCTGCGGTGTTTTTCGGCTGCACTTTTCGTCGCGTTCCGC
CCGGCCTTCGCGCTTTTCTTGATCACTGTGGCTGGGGACCGCTTCGCGTTATCATCCTGGT
CGCAGGGGCATTTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTCTGGTTTCATCTTGG
TCCATGTGACCGACCGGTGAGATGCCCGGCTCCAGTACGGCCTCCTGATTTTTGGTGCTGCT
GTCTCTGTCTTCTACAGGAGGTGTTCCGCTTTGCCTACTACAAGCTGCTTAAGAAGGCAGA
TGAAGGGTTAGCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCCGCCAGATGGCCT
ATGTTTCTGGTCTCTCCTTCGGTATCATCAGTGGTGTCTTCTCTGTTATCAATATTTTGGCT
GATGCACTTTGGGCCAGGTGTGGTTGGGATCCATGGAGACTCACCTATTACTTCTTGACTTC
AGCCTTTCTGACAGCAGCCATTATCCTGCTCCATACTTTTGGGGAGTTGTGTTCTTTGATG
CCTGTGAGAGGAGACGGTACTGGGCTTTGGGCCTGGTGGTTGGGAGTCACCTACTGACATCG
GGACTGACATTCCTGAACCCCTGGTATGAGGCCAGCCTGCTGCCCATCTATGCAGTCACTGT
TTCCATGGGGCTCTGGGCCTTCATCACAGCTGGAGGGTCCCTCCGAAGTATTACAGCGCAGCC
TCTTGTGTAAGGACTGACTACCTGGACTGATCGCCTGACAGATCCACCTGCCTGTCCACTG
CCCATGACTGAGCCCAGCCCCAGCCCCGCTCCATTGCCACATTCTCTGTCTCCTTCTCGTC
GGTCTACCCCACTACCTCCAGGGTTTGTCTTTGTCTTTTGTGACCGTTAGTCTCTAAGCTT
TACCAGGAGCAGCCTGGGTTTCAGCCAGTCACTGAGTGGTGGGTTTGAATCTGCACTTATCCC
CACCACCTGGGGACCCCCCTTGTGTGTCCAGGACTCCCCCTGTGTCACTGCTCTGCTCTCAC
CCTGCCCAAGACTCACCTCCCTTCCCTCTGTCAGGCCGACGGCAGGAGGACAGTCGGGTGAT
GGTGTATTCTGCCCTGCGCATCCACCCGAGGACTGAGGGAAACCTAGGGGGGACCCCTGGGC
CTGGGGTGCCCTCCTGATGTCTCGCCCTGTATTTCTCCATCTCCAGTTCTGGACAGTGCAG
GTTGCCAAAGAAAAGGGACCTAGTTTAGCCATTGCCCTGGAGATGAAATTAATGGAGGCTCAA
GGATAGATGAGCTCTGAGTTTCTCAGTACTCCCTCAAGACTGGACATCTTGGTCTTTTTCTC
AGGCCTGAGGGGGAACCATTTTTGGTGTGATAAATACCCTAAACTGCCTTTTTTTCTTTTTT
GAGGTGGGGGAGGGAGGAGGTATATTGGAACCTTCTAACCCTCCTTGGGCTATATTTCTC
TCTCGAGTTGCTCCTCATGGCTGGGCTCATTTGGTCCCTTTCTCCTTGGTCCCAGACCTT
GGGGGAAAGGAAGGAAGTGCATGTTTGGGAACCTGGCATTACTGGAACATAATGGTTTTAACCT
CCTTAACCACCAGCATCCCTCCTCTCCCCAAGGTGAAGTGGAGGGTGTCTGTGGTGAGCTGGC
CACTCCAGAGCTGCAGTGCCACTGGAGGAGTCAGACTACCATGACATCGTAGGGAAGGAGGG
GAGATTTTTTTGTAGTTTTTAATTGGGGTGTGGGAGGGGCGGGGAGTTTTCTATAAACTGT
ATCATTTTCTGCTGAGGGTGGAGTGTCCCATCCTTTTAATCAAGGTGATTGTGATTTTGACT
AATAAAAAAGAATTTGTAAAAA
AAAAA

FIGURE 220

MGA AVFFGCTFVAFGPAFALFLITVAGDPLRVIIILVAGAFFWLVSLLLASVVWFILVHVTDR
SDARLQYGLLIFGAAVSVLLQEVFRFAYYKLLKKADEGLASLSEDGRSPISIRQMAYVSGLS
FGIISGVFSVINILADALGPGVVGIIHGDSPIYFLTSAFLTAIIILLHTFWGVVFFDACERRR
YWALGLVVGSHLLTSGLTFLNPWYEASLLPIYAVTVSMGLWAFITAGGSLRSIQRSLCKD

FIGURE 221

AAGCTGGTTTAAAGGAAGCAGAGGAGGGTTAGATTTCGTTGAGTGAGGACGGAAGATCAACCCA
TTTCCATTCCGCCAGATGGCCTATGTTTCTGGTCTCTCCCTTCGGNATCATCAGTGGTGTNT
TNTCTGTTATCAATATTTTGGCTGATGCANTTGGGCCAGGTGTGGTTGGGATCCATGGAGAC
TCACCCTATTANTTCCTGANTTCAGCCTTTNTGACAGCAGCCATTATCCTGCTC

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FIGURE 222

GACCGACCGTTCAGATGCCCCGGTTCAGTACGGCTTCCTGATTTTTGGTGCTGCTGTNTCTG
TCCTTCTACAGGAGGTGTTCCGCTTTGCCTANTACAAGCTGCTTAAGAAGGCAGATGAGGGG
TTAGCATNGCTGAGTGAGGACGGAAGATCACCCATTTCCATCCGCCAGATGGCCTATGTTTN
TGGTNTTTCCTTCGGTATCATCAGTGGTGTTTTNTCTGTTATCAATATTTTGGNTGATGCAN
TTGGGCCAGGTGTGGTTGGGATCCATGGAGANTCACCCCTATTAATTCCTGAATTCAGCCTTT
NTGACAGCAGCCATTATCCTGNTCCATACCTTTTGGGGAGTTGTGTTTTTTGATGCCTGTGA
GAGGAG

FIGURE 223

NGTTGGAGAAGTGGCGCGGACNTTCATTTGGGGTTTCGGTTTCCCCCCTTTCCTTTCCCCG
GGGTCTGGGGTGACATTGCACGGGCCCCCTCGTGGGGTCGCGTTGCCACCCACGCGGACTCC
CCAGNTGGNGCGCCCTTCCCATTTCCTGTCTGGTCAGGCCCCACCCCCCTTCCCACNTG
ACCAGCCATGGGGGCTGCGGTGTTTTTCGGCTGCACTTTCGTGCGGTTCGGCCCGGCCTTCG
CGCTTTTCTTGATCACTGTGGCTGGGGACCCGCTTCGCGTTATCATCCTGGTCGCAGGGGCA
TTTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTCTGGTTCATCTTGGTCCATGTGAC
CGACCGGTGAGATGCCCCGGCTCCAGTACGGCCTCCTGATTTTTGGTGCTGCTGTCTCTGTCC
TTCTACAGGAGGTGTTCCGCTTTGCCTACTACAAGCTGCTTAAGAAGGCAGATGAGGGGTTA
GCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCCGCCAGATGGCCTATGTTTCTGG
TCTCTCCTTCGGTATCATCAGTGGTGTCTTCTCTGTTATCAATATTTTGGCTGATGCACTTG
GGCCAGGTGTGGTTGGGATCCATGGAGACTCACCC

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FIGURE 224

GTAAAAGAAAAGTGGCCGGACCTTCATTGGGGTTTCGGTTCCCCCCTTCCCNTTCCCCGGGG
TCTGGGGGTGACATTGCACCGCGCCCNCTCGTGGGGTCGCGTTGCCACCCACGCGGACTCCC
CAGNTGGCGCGCCCCCTCCCATTTGCCTGTCCTGGTCAGGCCCCACCCCCCTTCCCACCTGA
CCAGCCATGGGGGCTGCGGTGTTTTTCGGGCTGCACTTTCGTGCGGTTCGGGCCCGGCCTTC
GCGCTTTTCTTGATCACTGTGGCTGGGGACCCGCTTCGCGTTATCATCCTGGTCGCAGGGGC
ATTTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTCTGGTTCATCTTGGTCCATGTGA
CCGACCGGTCAGATGCCCCGGCTCCAGTACGGCCTCCTGATTTTTTGGTGCTGCTGTCTCTGTC
CTTCTACAGGAGGTGTTCCGCTTTGCCTACTACAAGCTGCTTAAGAAGGCAGATGAGGGGTT
AGCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCCGCCAGATGGCCTATGTTTCTG
GTCTCTCCTTCGGTATCATCAGTGGTGTCTTCTCTGTTATCAATATTTTGGCTGATGCACTT
GGGCCAGGTGTGGTTGGGATCCATGGAGAC

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FIGURE 225

GGCCCAGGGAGCAGTGGGTGGTTATAACTCAGGCCCGGTGCCCAGAGCCCAGGAGGAGGCAG
TGGCCAGGAAGGCACAGGCCTGAGAAGTCTGCGGCTGAGCTGGGAGCAAATCCCCACCCCC
TACCTGGGGGACAGGGCAAGTGAGACCTGGTGAGGGTGGCTCAGCAGGCAGGGAAGGAGAGG
TGTCTGTGCGTCCTGCACCCACATCTTTCTCTGTCCCCCTCCTTGCCCTGTCTGGAGGCTGCT
AGACTCCTATCTTCTGAATTCTATAGTGCTGGGTCTCAGCGCAGTGCCGATGGTGGCCCCGT
CCTTGTGGTTCTCTCTACCTGGGGAAATAAGGTGCAGCGGCCATGGCTACAGCAAGACCCC
CCTGGATGTGGGTGCTCTGTGCTCTGATCACAGCCTTGCTTCTGGGGGTACAGAGCATGTT
CTCGCCAACAATGATGTTTCTGTGACCACCCCTCTAACACCGTGCCCTCTGGGAGCAACCA
GGACCTGGGAGCTGGGGCCGGGGAAGACGCCCCGTGGGATGACAGCAGCAGCCGCATCATCA
ATGGATCCGACTGCGATATGCACACCCAGCCGTGGCAGGCCGCGCTGTTGCTAAGGCCCAAC
CAGCTCTACTGCGGGCGGTGTTGGTGCATCCACAGTGGCTGCTCACGGCCGCCCCACTGCAG
GAAGAAAGTTTTTCAGAGTCCGTCTCGGCCACTACTCCCTGTCACCAGTTTATGAATCTGGGC
AGCAGATGTTCCAGGGGTCAAATCCATCCCCACCCCTGGCTACTCCCACCCCTGGCCACTCT
AACGACCTCATGCTCATCAAACCTGAACAGAAGAATTGTCCTCCACTAAAGATGTCAGACCCAT
CAACGTCTCCTCTCATTGTCCCTCTGCTGGGACAAAGTGCTTGGTGTCTGGCTGGGGGACAA
CCAAGAGCCCCCAAGTGCACTTCCCTAAGGTCCTCCAGTGCTTGAATATCAGCGTGCTAAGT
CAGAAAAGGTGCGAGGATGCTTACCCGAGACAGATAGATGACACCATGTTCTGCGCCGGTGA
CAAAGCAGGTAGAGACTCCTGCCAGGGTGATTCTGGGGGGCCTGTGGTCTGCAATGGCTCCC
TGCAGGGACTCGTGTCCTGGGGAGATTACCCTTGTGCCCCGCCCAACAGACCGGGTGTCTAC
ACGAACCTCTGCAAGTTCACCAAGTGGATCCAGGAAACCATCCAGGCCAACTCCTGAGTCAT
CCCAGGACTCAGCACACCGGCATCCCCACCTGCTGCAGGGACAGCCCTGACACTCCTTTTCAG
ACCCTCATTCCTTCCCAGAGATGTTGAGAATGTTTCATCTCTCCAGCCCCTGACCCCATGTCT
CCTGGACTCAGGGTCTGCTTCCCCACATTGGGCTGACCGTGTCTCTCTAGTTGAACCCCTGG
GAACAATTTCCAAAACGTCCAGGGCGGGGGTTCGTCTCAATCTCCCTGGGGCACTTTTCAT
CCTCAAGCTCAGGGCCCCATCCCTTCTCTGCAGCTCTGACCCAAATTTAGTCCCAGAAATAAA
CTGAGAAGTGGAAAAAAAAA

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FIGURE 226

MATARPPMMWVLCALITALLLGVTEHVLANNVSCDHPSNTVPSGSNQDLGAGAGEDARSDD
SSSRIINGSDCDMHTQPWQAALLLRPNQLYCGAVLVHPQWLLTAAHCRKKVFRVRLGHYSLS
PVYESGQQMFQGVKSI PHPGYSHPGHSNDLMLIKLNRRI RPTKDVRPINVSSHCP SAGTKCL
VSGWGTTKSPQVHF PKVLQCLNISVLSQKRCEDAYPRQIDDTMFCAGDKAGR DSCQGD SGGP
VVCNGSLQGLVSWGDYPCARPNRPGVYTNLCKFTKWIQETIQANS

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FIGURE 227

ATGGTCAACGACCGGTGGAAGACCATGGGCGGCGCTGCCAACTTGAGGACCGGCCGCGCGA
CAAGCCGACGCGGCCGAGCTGCGGGCTACGTGCTGTGCACCGTGTCTGGCCCTGGCTGTGC
TGCTGGCTGTAGCTGTCAACGGTGCCGTGCTCTTCTGAACCAAGCCACGCGCCGGGCACG
GCGCCCCACCTGTCTGTAGCACTGGGGCTGCCAGCGCCAACAGCGCCCTGGTCACTGTGGA
AAGGGCGGACAGCTCGCACCTCAGCATCCTCATTGACCCGCGCTGCCCCGACCTCACCGACA
GCTTCGCACGCTGGAGAGCGCCAGGCCTCGGTGCTGCAGGCGCTGACAGAGCACCAGGCC
CAGCCACGGCTGGTGGGCGACAGGAGCAGGAGCTGCTGGACACGCTGGCCGACCAGCTGCC
CCGGCTGTGGCCGAGCCTCAGAGCTGCAGACGAGTGCAATGGGCTGCGGAAGGGGCATG
GCACGCTGGGCCAGGGCCTCAGCGCCTGCAGAGTGAGCAGGGCCGCTCATCCAGCTTCTC
TCTGAGAGCCAGGGCCACATGGCTCACCTGGTGAACCTCCGTGACGACATCCTGGATGCCCT
GCAGAGGGACCGGGGGCTGGGCCGGCCCCGCAACAAGGCCGACCTTCAGAGAGCGCCTGCC
GGGGAACCCGGCCCCGGGGCTGTGCCACTGGCTCCCGCCCCGAGACTGTCTGGACGTCTCT
CTAAGCGGACAGCAGGACGATGGCGTCTACTGTCTTTCCACCCACTACCCGGCCGGCTT
CCAGGTGTACTGTGACATGCGCACGGACGGCGGGCTGGACGGTGTTCAGCGCCGGGAGG
ACGGCTCCGTGAACCTTCTCCGGGGCTGGGACGCGTACCGAGACGGCTTTGGCAGGCTCACC
GGGGAGCACTGGCTAGGGCTCAAGAGGATCCACGCCCTGACCACACAGGCTGCCTACGAGCT
GCACGTGGACCTGGAGGACTTTGAGAATGGCACGGCCTATGCCCGCTACGGGAGCTTCGGCG
TGGGCTTGTCTCCGTGGACCTGAGGAAGACGGGTACCCGCTCACCGTGGCTGACTATTCC
GGCACTGCAGGCGACTCCCTCCTGAAGCACAGCGGCATGAGGTTCAACCACCAAGGACCGTGA
CAGCGACCATTCAGAGAACAACCTGTGCCGCTTCTACCGCGGTGCCTGGTGGTACCGCAACT
GCCACACGTCCAACCTCAATGGGCAGTACCTGCGCGGTGCGCACGCCTCCTATGCCGACGGC
GTGGAGTGGTCTCCTGGACCGCTGGCAGTACTCACTCAAGTTCTCTGAGATGAAGATCCG
GCGGCTCCGGGAGGACCGCTAGACTGGTGCACCTTGTCTTGGCCCTGCTGGTCCCTGTGCG
CCCATCCCCGACCCACCTCACTCTTTCGTGAATGTTCTCCACCCACCTGTGCCTGGCGGAC
CCACTCTCCAGTAGGGAGGGGCCGGGCCATCCCTGACACGAAGCTCCCTGGGCCGGTGAAGT
CACACATCGCCTTCTCGCCGTCCCCACCCCTCCATTGGCAGCTCACTGATCTCTTGCCCT
TGCTGATGGGGCTGGCAAACCTTGACGACCCCAACTCCTGCCTGCCCCACTGTGACTCCGG
TGCTGTTTGCCGTCCCCCTGGCCAGGATGGTGGAGTCTGCCCCAGGCACCCCTCTGCCCTGCC
GGCCAAATACCCGCATTATGGGGACAGAGAGCAGGGGGCAGACAGCACCCTGGAGTCTCTC
CTAGCAGATCGTGGGGAATGTAGGTCTCTCTGAGGTGAGGTCTGAGGCCAGTATCCTCCAG
CCCTCCCAATGCCAACCCCAACCCGTTTCCCTGGTGCCCAGAGAACCCACCTCTCCCCCAA
GGGCCTCAGCCTGGCTGTGGCTGGGTGGCCCCATCCTACCAGGCCCTGAGGTGAGGATGGG
GAGCTGCTGCCTTTGGGGACCCACGCTCCAAGGCTGAGACCAGTTCCCTGGAGGCCACCCAC
CCTGTGCCCCGGCAGGCCTGGGGTCTGCAGTCTCTTACCTGCTGTGCCACCTGCTCTCTG
TCTCAAATGAGGCCCAACCCATCCCCACCCAGCTCCCGGCCGTCTCTACCTGGGGCAGC
CGGGGCTGCCATCCCATTCTCTGCCTCTGGAAGGTGGGTGGGCCCTGCACCGTGGGGCT
GGACTGCGCTAATGGGAAGCTCTTGGTTTTCTGGGCTGGGGCTAGGCAGGGCTGGGATGAG
GCTTGTACAACCCCAACCAATTTCCAGGGACTCCAGGGTCTGAGGCCTCCAGGAGG
GCCTTGGGGGTGATGACCCCTTCCCTGAGGTGGCTGTCTCCATGAGGAGGCCAACCTTGCC
ATTGACCGTGGCCACCTGGACCCAGGCCAGGCCGGCCGGCCGAGTGGTCAAGGGACAGGGA
CCACCTCACCGGGCAAATGGGGTGGGGGGACTGGGGCACCAGACCAGGCACCACTGGACA
CTTTCTTGTGAATCCTCCCAACACCCAGCACGCTGTATCCCCACTCCTTGTGTGCACACA
TGCAGAGGTGAGACCCGAGGCTCCCAGGACCAGCAGCCACAAGGGCAGGGCTGGAGCCGGG
TCCTCAGCTGTCTGCTCAGCAGCCCTGGACCCGCGTGCGTTACGTGAGGCCAGATGCAGGG
CGGCTTTTCCAAGGCCTCCTGATGGGGCCCTCCGAAAGGCTGGAGTCAGCCTTGGGGAGCT
GCCTAGCAGCCTCTCCTCGGGCAGGAGGGGAGGTGGCTTCTCCAAAGGACACCCGATGGCA
GGTGCTAGGGGGTGTGGGGTCCGTTCTCCCTTCCCTCCCACTGAAGTTTGTGCTTAAAA
AACAATAAATTTGACTTGGCACCCTGGGGGTTGGTGGGAGAGGCCGTGTGACCTGGCTCTC
TGTCCAGTGCCACCAGGTCATCCACATGCGCAG

FIGURE 228

MVNDRWKTMGGAAQLEDPRDKPQRPSCGYVLCTVLLALAVLLAVAVTGAVLFLNHAHAPGT
APPPVVSTGAASANSALVTVERADSSHLSILIDPRCPDLTDSFARLESAQASVLQALTEHQA
QPRLVGDQEQELDLADQLPRLRLARASELQTECMGLRKGHGTLGQGLSALQSEQGRLIQLL
SESQGHMAHLVNSVSDILDALQDRGLGRPRNKADLQRAPARGTRPRGCATGSRPRDCLDVL
LSGQQDDGVYSVFPPTHYPAGFQVYCDMRDGGGWTVFQRREDGSVNFFRGWDAYRDGFGRLT
GEHWLGLKRIHALTTQAAYELHVDLEDFENGTAARYGSFGVGLFSVDPEEDGYPLTVADYS
GTAGDSLLKHSGMRFTTKDRSDHSENNCAAFYRGAWWYRNCHTSNLNGQYLRGAHASADG
VEWSSWTGWQYSLKFSEMKIRPVREDR

FIGURE 229

GCAGTCAGAGACTTCCCCTGCCCCTCGCTGGGAAAGAACATTAGGAATGCCTTTTAGTGCCT
TGCTTCCTGAACTAGCTCACAGTAGCCCGGCGGCCAGGGCAATCCGACCACATTTCACTCT
CACCGCTGTAGGAATCCAGATGCGAGGCCAAGTACAGCAGCACGAGGGACATGCTGGATGATG
ATGGGGACACCACCATGAGCCTGCATTCTCAAGCCTCTGCCACAACCTCGGCATCCAGAGCCC
CGGCGCACAGAGCACAGGGCTCCCTCTTCAACGTGGCGACCAGTGGCCCTGACCCTGCTGAC
TTTGTGCTTGGTGCTGCTGATAGGGCTGGCAGCCCTGGGGCTTTTGTTTTTTCAGTACTACC
AGCTCTCCAATACTGGTCAAGACACCATTTCTCAAATGGAAGAAAGATTAGGAAATACGTCC
CAAGAGTTGCAATCTCTTCAAGTCCAGAATATAAAGCTTGCAGGAAGTCTGCAGCATGTGGC
TGAAAACTCTGTCGTGAGCTGTATAACAAAGCTGGAGCACACAGGTGCAGCCCTTGTACAG
AACAATGGAATGGCATGGAGACAATTGCTACCAGTTCTATAAAGACAGCAAAAGTTGGGAG
GACTGTAAATATTTCTGCCTTAGTGAAAACTCTACCATGCTGAAGATAAAACAAACAAGAAGA
CCTGGAATTTGCCGCTCTCAGAGCTACTCTGAGTTTTTCTACTCTTATTGGACAGGGCTTT
TGCGCCCTGACAGTGGCAAGGCCTGGCTGTGGATGGATGGAACCCCTTTCACTTCTGAACTG
TTCCATATTATAATAGATGTCACCAGCCCAAGAAGCAGAGACTGTGTGGCCATCCTCAATGG
GATGATCTTCTCAAAGGACTGCAAAGAATTGAAGCGTTGTGTCTGTGAGAGAAGGGCAGGAA
TGGTGAAGCCAGAGAGCCTCCATGTCCCCCTGAAACATTAGGCGAAGGTGACTGATTGCCC
CTCTGCAACTACAAATAGCAGAGTGAGCCAGGCGGTGCCAAAGCAAGGGCTAGTTGAGACAT
TGGGAAATGGAACATAATCAGGAAAGACTATCTCTCTGACTAGTACAAAATGGGTTCTCGTG
TTTCCTGTTTCAAGATCACCAGCATTTCTGAGCTTGGGTTTATGCACGTATTTAACAGTCACA
AGAAGTCTTATTTACATGCCACCAACCAACCTCAGAAACCATAATGTCATCTGCCTTCTTG
GCTTAGAGATAACTTTTAGCTCTCTTCTCTCAATGTCTAATATCACCTCCCTGTTTTTCAT
GTCTTCCTTACACTTGGTGGAAATAAGAACTTTTTGAAGTAGAGGAAATACATTGAGGTAAC
ATCCTTTTCTCTGACAGTCAAGTAGTCCATCAGAAATTGGCAGTCACTTCCCAGATTGTACC
AGCAAATACACAAGGAATCTTTTTGTTTGTTCAGTTCATACTAGTCCCTTCCCAATCCAT
CAGTAAAGACCCCATCTGCCTTGTCCATGCCGTTTCCCAACAGGGATGTCACTTGATATGAG
AATCTCAAATCTCAATGCCTTATAAGCATTCTTCTGTGTCCATTAAAGACTCTGATAATTG
TCTCCCTCCATAGGAATTTCTCCCAGGAAAGAAATATATCCCCATCTCCGTTTCATATCAG
AACTACCGTCCCCGATATTCCCTTCAGAGAGATTAAAGACCAGAAAAAAGTGAGCCTCTTCA
TCTGCACCTGTAATAGTTTCAGTTCCTATTTTCTTCCATTGACCCATATTTATACCTTTTCAG
GTACTGAAGATTTAATAATAATAAATGTAAATACTGTGAAAAA

FIGURE 230

MQAKYSSTRDMLDDDGDTTMSLHSQASATTRHPEPRRTEHRAPSSTWRPVALTLLTLCLVLL
IGLAALGLLFFQYYQLSNTGQDTISQMEERLGNTSQELQSLQVQNIKLAGSLQHVAEKLCRE
LYNKAGAHRCSPCTEQWKWHGDNCYQFYKDSKSWEDCKYFCLSENSTMLKINKQEDLEFAAS
QSYSEFFYSYWTGLLRPD SGKAWLWMDGTPFTSELFHIIIDVTSPRSRDCVAILNGMIFSKD
CKELKRCVCERRAGMVKPESLHVPPETLGED

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FIGURE 231

AATTTTCACCGCTGTAGGAATCCAGATGCAGGCCAAGTACAGCAGCACGAGGGACATGNTGG
ATGATGATGGGACACCACCATGAGCCTGCATTNTCAAGCTTTTGCCACAATTCTGGCATCCAG
AGCCCCGGCGCACAGAGCACAGGGNTCCTTTTTCAACGTGGCGACCAGTGGCCCTGACCCTG
CTGACTTTGTGCTTGGTGCTGCTGATAGGGCTGGCAGCCCTGGGGCTTTTGTTTTTTTCAGTA
CTACCAGCTCTCCAATACTGGTCAAGACACCATTTCTCAAATGGAAGAAAGATTAGGAAATA
CGTCCCAAGAGTTGCAATTTNTTCAAGTCCAGAATATAAAGCTTGCAGGAAGTNTGCAGCAT
GTGGCTGAAAACTCTGTCGTGAGCTGTATAACAAAGCTGGAGGAACTTTGAAGGAGGGCAA
AGTNTCCTCATNTACTATACACACACCACTTCCC

FIGURE 232

GCCGAGCGCAAGAACCCTGCGCAGCCCAGAGCAGCTGCTGGAGGGGAATCGAGGCGCGGCTC
CGGGGATTCGGCTCGGGCCGCTGGCTCTGCTCTGCGGGGAGGGAGCGGGCCCCCGCGGGG
CCCCGAGCCCTCCGGATCCGCCCCCTCCCCGGTCCCCCCCCCTCGGAGACTCCTCTGGCTGCT
CTGGGGGTTCGCCCGGGGCGGGGACCCGCGGTCCGGGCGCCATGCGGGCATCGCTGCTGCTG
TCGGTGCTGCGGCCCGCAGGGCCCCGTGGCCGTGGGCATCTCCCTGGGCTTCACCCTGAGCCT
GCTCAGCGTCACCTGGGTGGAGGAGCCGTGCGGCCCAGGCCCCGCCAACCTGGAGACTCTG
AGCTGCCGCCGCGCGGCAACACCAACGCGGCGCGCCGCCAACCTCGGTGCAGCCCCGAGCG
GAGCGCGAGAAGCCCGGGGCGGGCGAAGGCGCCGGGAGAATTGGGAGCCGCGCGTCTTGCC
CTACCACCCCTGCACAGCCCGGCCAGGCCGCCAAAAAGGCCGTGAGGACCCGCTACATCAGCA
CGGAGCTGGGCATCAGGCAGAGGCTGCTGGTGGCGGTGCTGACCTCTCAGACCACGCTGCCC
ACGCTGGGCGTGGCCGTGAACCGCACGCTGGGGCACCGGCTGGAGCGTGTGGTGTTCCTGAC
GGGCGCACGGGGCCGCGGGCCCCACCTGGCATGGCAGTGGTGACGCTGGGCGAGGAGCGAC
CCATTGGACACCTGCACCTGGCGCTGCGCCACCTGCTGGAGCAGCACGGCGAGACTTTGAC
TGTTCTTCTGGTGCTGACACCACCTACACCGAGGCGCACGGCCTGGCACGCCTAACTGG
CCACCTCAGCCTGGCCTCCGCCGCCACCTGTACCTGGGCCGGCCCCAGGACTTCATCGGCG
GAGAGCCCCACCCCGGCCGCTACTGCCACGGAGGCTTTGGGGTGCTGCTGTGCGCATGCTG
CTGCAACAACCTGCGCCCCACCTGGAAGGCTGCCGCAACGACATCGTCAGTGCGCGCCCTGA
CGAGTGGCTGGGTGCTGCAATCTCGATGCCACCGGGGTGGGCTGCACTGGTGACCACGAGG
GGGTGCACTATAGCCATCTGGAGCTGAGCCCTGGGGAGCCAGTGCAAGAGGGGGACCTCAT
TTCCGAAGTGCCCTGACAGCCCACCTGTGCGTGACCCTGTGCACATGTACCAGCTGCACAA
AGCTTTCGCCCAGCTGAACTGGAACGCACGTACCAGGAGATCCAGGAGTTACAGTGGGAGA
TCCAGAATACCAGCCATCTGGCCGTTGATGGGGACCGGGCAGCTGCTTGGCCCCGTGGTATT
CCAGCACCATCCCGCCCGGCCCTCCCGCTTTGAGGTGCTGCGCTGGGACTACTTCACGGAGCA
GCACGCTTTCTCCTGCGCCGATGGCTCACCCCGCTGCCCACTGCGTGGGGCTGACCGGGCTG
ATGTGGCCGATGTTCTGGGGACAGCTCTAGAGGAGCTGAACCGCCGCTACCACCCGGCCTTG
CGGCTCCAGAAGCAGCAGCTGGTGAATGGCTACCGACGCTTTGATCCGGCCCGGGGTATGGA
ATACACGCTGGACTTGACAGCTGGAGGCACTGACCCCCCAGGGAGGCCGCCGCCCTCACTC
GCCGAGTGCACTGCTCCGGCCGCTGAGCCGCGTGGAGATCTTGCTGTGCCCTATGTCACT
GAGGCCTCACGTCTCACTGTGCTGCTGCCCTCTAGCTGCGGCTGAGCGTGACCTGGCCCCCTGG
CTTCTTGGAGGCCTTTGCCACTGCAGCACTGGAGCCTGGTGATGCTGCGGCAGCCCTGACCC
TGCTGCTACTGTATGAGCCGCGCCAGGCCCAGCGCGTGGCCCATGCAGATGTCTTCGCACCT
GTCAAGGCCCCACGTGGCAGAGCTGGAGCGGCGTTTCCCCGGTGCCCGGGTGCCATGGCTCAG
TGTGCAGACAGCCGCACCCCTACCACTGCGCCTCATGGATCTACTCTCCAAGAAGCACCCGC
TGGACACACTGTTCTGCTGGCCGGGCCAGACACGGTGCTCACGCCTGACTTCTGAACCGC
TGCCGCTATGCATGCCATCTCCGGCTGGCAGGCCTTCTTTCCCATGCATTTCCAAGCCTTCCA
CCAGGTGTGGCCCCACCACAAGGCGCTGGGCCCCCAGAGCTGGGCCGTGACACTGGCCGCT
TTGATCGCCAGGCAGCCAGCGAGGCTGCTTCTACAACCTCCGACTACGTGGCAGCCCGTGGG
CGCCTGGCGGCAGCCTCAGAACAAGAAGAGGAGCTGCTGGAGAGCCTGGATGTGTACGAGCT
GTTCTCTCACTTCTCCAGTCTGCATGTGCTGCGGGCGGTGGAGCCGGCGCTGCTGCAGCGCT
ACCGGGCCAGACGTGCAGCGCGAGGCTCAGTGAGGACCTGTACCACCGCTGCCCTCAGAGC
GTGCTTGAGGGCCTCGGCTCCCGAACCCAGCTGGCCATGCTACTCTTTGAACAGGAGCAGGG
CAACAGCACCTGACCCCCACCCCTGTCCCCGTGGGCCGTGGCATGGCCACACCCCACTT
CTCCCCAAAACAGAGCCACCTGCCAGCCTCGCTGGGCAGGGCTGGCCGTAGCCAGACCCC
AAGCTGGCCCACTGGTCCCTCTCTGGCTCTGTGGGTCCCTGGGCTCTGGACAAGCACTGGG
GGACGTGCCCCCAGAGCCACCCACTTCTCATCCCAAACCCAGTTTCCCTGCCCCCTGACGCT
GCTGATTGCGGCTGTGGCCTCCACGTATTTATGCAGTACAGTCTGCCTGACGCCAGCCCTGC
CTCTGGGCCCTGGGGCTGGGCTGTAGAAGAGTTGTGGGGAAGGAGGAGCTGAGGAGGGG
GCATCTCCCAACTTCTCCCTTTTGGACCCTGCCGAAGCTCCCTGCCTTTAATAAACTGGCCA
AGTGTGAAAAA

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FIGURE 233

MRASLLLSVLRPAGPVAVGISLGFTLSLLSVTWVEEPCGPGPPQPGDSELPPRGNTNAARRP
NSVQPGAEREKPGAGEGAGENWEPRVLPYHPAQPGQAAKKAVRTRYISTELGIRQLLVAVL
TSQTTLPTLGVAVNRTLGHRLERVVFLTGARGRRAPPGMAVVTLGEEPIGHLHLALRHLL
QHGDDEFDWFLLVPDTTYTEAHGLARLTGHLSLASAAHLYLGRPQDFIGGEPTPGRYCHGGFG
VLLSRMLLQQLRPHLEGCRNDIVSARPDEWLGRCILDATGVGCTGDHEGVHYSHLELSPGEP
VQEGDPHFRSALTAPVRDPVHMYQLHKAFARAELEPTYQEIQELQWEIQNTSHLAVDGDRA
AAWPVGIPAPSRPASRFEVLRWDYFTEQHAFSCADGSPRCPLRGADRADVADVLTAL EELN
RRYHPALRLQKQQLVNGYRRFDPARGMEYTLDLQLEALTPQGGRRPLTRRVQLLRPLSRVEI
LPVPYVTEASRLTVLLPLAAAERDLAPGFLEAFATAALEPGDAAAALTLLLLYEPRQAQRVA
HADVFAPVKAHVAELERRFPGARVPWLSVQTAAPSPLRLMDLLSKKHPLDTLFLLAGPDTV
TPDFLNRCRMHAISGWQAFFPMHFQAFHPGVAPPQPGPPPELGRDTGRFDRQAASEACFYNS
DYVAARGRLAAASEQEEELLES LDVYELFLHFSSHLVLR AVEPALLQRYRAQTCSARLSEDL
YHRCLQSVLEGLGSRTQLAMLLFEQE QGNST

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FIGURE 234

GCTCTGGCCGGCCCCGGCGATTGGTCACCGCCCGCTAGGGGACAGCCCTGGCCTCCTCTGAT
TGGCAAGCGCTGGCCACCTCCCCACACCCCTTGCGAACGCTCCCCTAGTGGAGAAAAGGAGT
AGCTATTAGCCAATTCGGCAGGGCCCCGCTTTTTAGAAAGCTTGATTTCTTTGAAGATGAAAG
ACTAGCGGAAGCTCTGCCTCTTTCCCCAGTGGGCGAGGGAACTCGGGGCGATTGGCTGGGAA
CTGTATCCACCCAAATGTCACCGATTTCTTCTTATGCAGGAAATGAGCAGACCCATCAATAA
GAAATTTCTCAGCCTGGCCGAAAAATGGTTGGCCCCACGAAGCCACGACAACCTGGAGGCAAAG
AGGGTTGCTCAACGCCCCGCCTCATTGGAAAACCAAATCAGATCTGGGACCTATATAGCGTG
GCGGAGGCGGGCGATGATTGTCGCGCTCGCACCCACTGCAGCTGCGCACAGTCGCATTTCT
TTCCCCGCCCTGAGACCCTGCAGCACCATCTGTCTATGGCGGCTGGGCTGTTTGGTTTGAGC
GCTCGCCGTCTTTTGGCGGCAGCGGCGACGCGAGGGCTCCCGGCCGCCCGCGTCCGCTGGGA
ATCTAGCTTCTCCAGGACTGTGGTCGCCCCGTCCGCTGTGGCGGGAAAGCGGCCCCCAGAAC
CGACCACACCGTGGCAAGAGGACCCAGAACCCGAGGACGAAAACCTTGTATGAGAAGAACCCA
GACTCCCATGGTTATGACAAGGACCCCGTTTTGGACGTCTGGAACATGCGACTTGTCTTCTT
CTTTGGCGTCTCCATCATCCTGGTCCTTGGCAGCACCTTTGTGGCCTATCTGCCTGACTACA
GGATGAAAGAGTGGTCCCGCCGCGAAGCTGAGAGGCTTGTGAAATACCGAGAGGCCAATGGC
CTTCCCATCATGGAATCCAACCTGCTTCGACCCCAGCAAGATCCAGCTGCCAGAGGATGAGTG
ACCAGTTGCTAAGTGGGGCTCAAGAAGCACCGCCTTCCCCACCCCTGCCTGCCATTCTGAC
CTCTTCTCAGAGCACCTAATTAAAGGGGCTGAAAGTCTGAA

FIGURE 235

MAAGLFGLSARRLLAAAATRGLPAARVRWESSFSRTVVAPSAVAGKRPPEPTTPWQEDPEPE
DENLYEKNPDSHGYDKDPVLDVWNMRLVFFFGVSIILVLGSTFVAYLPDYRMKEWSRREAER
LVKYREANGLPIMESNCFDPSKIQLPEDE

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FIGURE 236

GGCGGCTGGGCTGTTTGGTTTGAGCGCTCGCCGTCTTTTGGCGGCAGCGGCGACGCGAGGGC
TCCCGGCCGCCCCGCTCCGCTGGGAATCTAGCTTCTCCAGGACTGTGGTCGCCCCGTCCGCT
GTGGCGGGAAAGCGGCCCCCAGAACCGACCACACCGTGGCAAGAGGACCCAGAACCCGAGGA
CGAAAAC TTGTATGAGAAGAACCAGACTCCCATGGTTATGACAAGGACCCCGTTTGGACG
TCTGGAACATGCGACTTGTCTTCTTCTTTGGCGTCTCCATCATCCTGGTCCTTGGCAGCACC
TTTGTGGCCTATCTGCCTGACTACAGGATGAAAGAGTGGTCCCGCCGCGAAGCTGAGAGGCT
TGTGAAATACCGAGAGGCCAATGGCCTTCCCATCATGGAATCCAAC TGCTTCGACCCAGCA
AGATCCAG

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FIGURE 237

GCGGCGGCTATGCGCTTGCTCTGCTCGTCCTGTTGCTCCTGGGGCCCGGCGGCTGGTGCCT
TGCAGAACCCCAACGCGACAGCCTGCGGGAGGAACTTGTATCACCCTGCTTCCGGGG
ACGTAGCCGCCACATTCCAGTTCCGACGCGCTGGGATTTCGGAGCTTCAGCGGGAAGGAGTG
TCCCATTACAGGCTCTTTCCCAAAGCCCTGGGGCAGCTGATCTCCAAGTATTCTCTACGGGA
GCTGCACCTGTCAATTCACACAAGGCTTTTGAGGACCCGATACTGGGGGCCACCCTTCCTGC
AGGCCCCATCAGGTGCAGAGCTGTGGGTCTGGTTCCAAGACACTGTCACTGATGTGGATAAA
TCTTGGAAGGAGCTCAGTAATGTCCTCTCAGGGATCTTCTGCGCCTCTCTCAACTTCATCGA
CTCCACCAACACAGTCACTCCCACTGCCTCCTTCAAACCCCTGGGTCTGGCCAATGACACTG
ACCACTACTTTCTGCGCTATGCTGTGCTGCCGCGGGAGGTGGTCTGCACCGAAAACCTCACC
CCCTGGAAGAAGCTCTTGCCCTGTAGTTCCAAGGCAGGCCTCTCTGTGCTGCTGAAGGCAGA
TCGCTTGTTCCACACCAGCTACCACTCCCAAGGCAGTGCATATCCGCCCTGTTTGCAGAAATG
CACGCTGTACTAGCATCTCCTGGGAGCTGAGGCAGACCCTGTCAGTTGTATTTGATGCCTTC
ATCACGGGGCAGGGAAAGAAAGACTGGTCCCTCTCCGGATGTTCTCCCGAACCCCTCACGGA
GCCCCGCCCCCTGGCTTCAGAGAGCCGAGTCTATGTGGACATCACCACTACAACCAGGACA
ACGAGACATTAGAGGTGCACCCACCCCCGACCACTACATATCAGGACGTCACTCTAGGCACT
CGGAAGACCTATGCCATCTATGACTTGCTTGACACCGCCATGATCAACAACCTCTCGAAACCT
CAACATCCAGCTCAAGTGGAAGAGACCCCCAGAGAATGAGGCCCCCCCCAGTGCCCTTCCTGC
ATGCCCAGCGGTACGTGAGTGGCTATGGGCTGCAGAAGGGGGAGCTGAGCACACTGCTGTAC
AACCCCCACCCATACCGGGCCTTCCCGGTGCTGCTGCTGGACACCGTACCCTGGTATCTGCG
GCTGTATGTGCACACCCTCACCATCACCTCCAAGGGCAAGGAGAACAAACCAAGTTACATCC
ACTACCAGCCTGCCCAGGACCGGCTGCAACCCACCTCCTGGAGATGCTGATTCAGCTGCCG
GCCAACTCAGTCACCAAGGTTTCCATCCAGTTTGAGCGGGCGCTGCTGAAGTGGACCGAGTA
CACGCCAGATCCTAACCATGGCTTCTATGTCAGCCCATCTGTCTCAGCGCCCTTGTGCCCA
GCATGGTAGCAGCCAAGCCAGTGGACTGGGAAGAGAGTCCCTCTTCAACAGCCTGTTCCCA
GTCTCTGATGGCTCTAACTACTTTGTGCGGCTCTACACGGAGCCGCTGCTGGTGAACCTGCC
GACACCGGACTTCAGCATGCCCTACAACGTGATCTGCCTCACGTGCACTGTGGTGGCCGTGT
GCTACGGCTCCTTCTACAATCTCCTCACCCGAACCTTCCACATCGAGGAGCCCCGCACAGGT
GGCCTGGCCAAGCGGCTGGCCAACCTTATCCGGCGCGCCGAGGTGTCCCCCACTCTGATT
CTTGCCCTTTCCAGCAGCTGCAGCTGCCGTTTCTCTCTGGGGAGGGGAGCCCAAGGGCTGTT
TCTGCCACTTGCTCTCCTCAGAGTTGGCTTTTGAACCAAAGTGCCCTGGACCAGGTGAGGGC
CTACAGCTGTGTTGTCCAGTACAGGAGCCACGAGCCAAATGTGGCATTGTAATTTGAATTAA
CTTAGAAATTCAATTCCTCACCTGTAGTGGCCACCTCTATATTGAGGTGCTCAATAAGCAAA
AGTGGTCCGTGGCTGCTGTATTGGACAGCACAGAAAAAGATTTCCATCACCAAGAAAGGTC
GGCTGGCAGCACTGGCCAAGGTGATGGGGTGTGCTACACAGTGTATGTCACTGTGTAGTGA
TGGAGTTTACTGTTTGTGGAATAAAAAACGGCTGTTTCCGTGGAACCAAAAAA

FIGURE 238

MPLALLVLLLLGPGGWCLAEPFRDSLREELVITPLPSGDVAATFCFRTRWDSELQREGVSHY
RLFPKALGQLISKYSLRELHLSFTQGFWRTYWGPPFLQAPSGAELWVWFQDTVTDVDSWK
ELSNVLSGIFCASLNFIDSTNTVTPTASFKPLGLANDTDHYFLRYAVLPREVVCTENLTPWK
KLLPCSSKAGLSVLLKADRLFHTSYHSQAVHIRPVCNARCTSSISWELRQTLSVVFDAFITG
QGKKDWSLFRMFSRTLTEPCPLASESRVYVDITTYNQDNETLEVHPPPTTTYQDVILGTRKT
YAIYDLLDTAMINNSRNLNIQLKWKRPENEAPPVPFLHAQRYVSGYGLQKGELSTLLYNTH
PYRAFPVLLLDTPWYLRLYVHTLTITSKGKENKPSYIHYQPAQDRLQPHLLEMLIQLPANS
VTKVSIQFERALLKWTEYTPDPNHGFYVSPSVLSALVPSMVAAPVDWEESPLFNSLFPVSD
GSNYFVRLYTEPLLVLNLPDPFSMPYNVICLTCTVVAVCYGSFYNNLLTRTFHIEEPRTGGLA
KRLANLIRRARGVPPL

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FIGURE 239

CAACAATGGGGTCCAGCAGCTTCTTGGTCCTCATGGTGTCTCTCGTTCTTGTGACCCTGGTGG
CTGTGGAAGGAGTTAAAGAGGGTATAGAGAAAGCAGGGGTTTGCCCAGCTGACAACGTACGC
TGCTTCAAGTCCGATCCTCCCCAGTGTACACAGACCAGGACTGTCTGGGGGAAAGGAAGTG
TTGTTACCTGCACTGTGGCTTCAAGTGTGTGATTCTGTGAAGGAACTGGAAGAAGGAGGAA
ACAAGGATGAAGATGTGTCAAGGCCATACCCTGAGCCAGGATGGGAGGCCAAGTGTCCAGGC
TCCTCCTCTACCAGGTGTCTCAGAAATGATGCTGGGTCTTTCTACCTCTGGGGGTCACTC
TCACTTGGCACCTGCCCCCTGAGGGTCCTGAGACTTGGAATATGGAAGAAGCAATACCCAACC
CCACCAAAGAAAACCTGAGCTTGAAGTCCTTTTCCCCAAAAAGAGGGAAGAGTCACAAAAAG
TCCAGACCCCAGGGACGGTACTTTCCCTCTCTACCTGGTGCTCCTCCCTAATGCTCATGAAT
GGACCCCTCATGAATGAAACCAGTGCCCTTATAAGAGACCCCAAAGAGCTGCCTTGCCCTTC
TGCAATGTGTGATCACAGCTAGAAGGCACTGTCAGAGAAGAGAAAAGTGGTCCTCACCAGATG
CTGAATCTGCTGGTGCCTTGATCTTGGACTTCCCAGCCTCTAGAACTGTAAGAAATAAATAT
TTGCTGTTTATAATCCAA

FIGURE 240

MGSSSFVLVLMVSLVLVTLVAVEGVKEGIEKAGVCPADNVRCFKSDPPQCHTDQDCLGERKCC
YLHCGFKCVIPVKELEEKGKDEDVSRPYPEPGWEAKCPGSSSTRCPQK

FIGURE 241

AAACTCAGCACTTGCCGGAGTGGCTCATTGTTAAGACAAAGGGTGTGCACTTCCTGGCCAGG
AAACCTGAGCGGTGAGACTCCCAGCTGCCTACATCAAGGCCCCAGGACATGCAGAACCTTCC
TCTAGAACCCGACCCACCACCATGAGGTCTGCCTGTGGAGATGCAGGCACCTGAGCCAAGG
CGTCCAGTGGTCTTGCTTCTGGCTGTCTGGTCTTCTTTCTCTTCGCCTTGCCCTCTTTTA
TTAAGGAGCCTCAAACAAAGCCTTCCAGGCATCAACGCACAGAGAACATTAAAGAAAGGTCT
CTACAGTCCCTGGCAAAGCCTAAGTCCCAGGCACCCACAAGGGCGAGGAGGACAACCATCTA
TGCAGAGCCAGCGCCAGAGAACAATGCCCTCAACACACAAACCCAGCCCAAGGCCCCACCA
CCGGAGACAGAGGAAAGGAGGCCAACAGGCACCGCCGGAGGAGCAGGACAAGGTGCCCCAC
ACAGCACAGAGGGCAGCATGGAAGAGCCAGAAAAAGAGAAAACCATGGTGAACACACTGTC
ACCCAGAGGGCAAGATGCAGGGATGGCTCTGGCAGGACAGAGGCACAATCATGGAAGAGCC
AGGACACAAAGACGACCCAAAGGAAATGGGGGCCAGACCAGGAAGCTGACGGCCTCCAGGACG
GTGTGAGAGAAGCACAGGGCAAAGCGGCAACCACAGCCAAGACGCTCATTCCCAAAAGTCA
GCACAGAATGCTGGCTCCACAGGAGCAGTGTCAACAAGGACGAGACAGAAAGGAGTGACCA
CAGCAGTCATCCACCTAAGGAGAAGAAACCTCAGGCCACCCACCCCTGCCCTTTCCAG
AGCCCCACGACGAGAGAAACCAAGACTGAAGGCCGCCAACTTCAAATCTGAGCCTCGGTG
GGATTTTGAGGAAAAATACAGCTTCGAAATAGGAGGCCTTCAGACGACTTGCCCTGACTCTG
TGAAGATCAAAGCCTCAAGTCGCTGTGGCTCCAGAACTCTTTCTGCCCAACCTCACTCTC
TTCCTGGACTCCAGACACTTCAACCAGAGTGAGTGGGACCGCCTGGAACACTTTGCACCACC
CTTTGGCTTCATGGAGCTCAACTACTCCTTGGTGCAGAAGGTCTGTACACGCTTCCCTCCAG
TGCCCCAGCAGCAGCTGCTCCTGGCCAGCCTCCCCGCTGGGAGCCTCCGGTGCATCACCTGT
GCCGTGGTGGGCAACGGGGGCATCCTGAACAACTCCACATGGGCCAGGAGATAGACAGTCA
CGACTACGTGTTCCGATTGAGCGGAGCTCTCATTAAAGGCTACGAACAGGATGTGGGGACTC
GGACATCCTTCTACGGCTTTACCGCCTTCTCCCTGACCCAGTCACTCCTTATATTGGGCAAT
CGGGGTTTCAAGAACGTGCCTCTTGGGAAGGACGTCCGCTACTTGCACTTCCTGGAAGGCAC
CCGGGACTATGAGTGGCTGGAAGCACTGCTTATGAATCAGACGGTGATGTCAAAAAACCTTT
TCTGGTTTCAGGCACAGACCCAGGAAGCTTTTCGGGAAGCCCTGCACATGGACAGGTACCTG
TTGCTGCACCCAGACTTTCTCCGATACATGAAGAACAGGTTTCTGAGGTCTAAGACCCTGGA
TGGTGCCCACTGGAGGATATACCGCCCCACCACTGGGGCCCTCCTGCTGCTCACTGCCCTTC
AGCTCTGTGACCAGGTGAGTGCTTATGGCTTCATCACTGAGGGCCATGAGCGCTTTTCTGAT
CACTACTATGATACATCATGGAAGCGGCTGATCTTTTACATAAACCATGACTTCAAGCTGGA
GAGAGAAGTCTGGAAGCGGCTACACGATGAAGGGATAATCCGGCTGTACCAGCGTCCTGGTC
CCGGAACCTGCCAAAGCCAAGAAGTGAACCGGGGCCAGGGCTGCCATGGTCTCCTTGCCCTGCTC
CAAGGCACAGGATACAGTGGGAATCTTGAGACTCTTTGGCCATTTCCCATGGCTCAGACTAA
GCTCCAAGCCCTTCAGGAGTTCCAAGGGAACACTTGAACCATGGACAAGACTCTCTCAAGAT
GGCAAATGGCTAATTGAGGTTCTGAAGTTCTTCAGTACATTGCTGTAGGTCTTGAGGCCAGG
GATTTTAAATTAATGAGGTTGATGGGTGGCCAATACCACAATTCTGCTGAAAAACACTCTT
CCAGTCCAAAAGCTTCTTGATACAGAAAAAGAGCCTGGATTTACAGAAACATATAGATCTG
GTTTGAATTCCAGATCGAGTTTACAGTTGTGAAATCTTGAAGGTATTACTTAACTTCACTAC
AGATTGTCTAGAAGACCTTTCTAGGAGTTATCTGATTCTAGAAGGGTCTATACTTGTCTTG
TCTTTAAGCTATTTGACAACTCTACGTGTTGTAGAAAACTGATAATAATACAAATGATTGTT
GTCCATGGAAAGGCAAATAAATTTTCTACAGTGAAAAA

FIGURE 242

MRSCLWRCRHLSQGVQWSLLLAVLVFFLFALPSFIKEPQTKPSRHQRTENIKERSLQSLAKP
KSQAPTRARRTTIYAEPAPENNALNTQTQPKAHTTGDRGKEANQAPPEEQDKVPHTAQRAAW
KSPEKEKTMVNTLSPRGQDAGMASGRTEAQSWKSQDTKTTQGNGGQTRKLTASRTVSEKHQG
KAATTAKTLIPKSQHRMLAPTGA VSTRTRQKGVTTAVIPPEKKKPQATPPPAPFQSPTTQRN
QRLKAANFKSEPRWDFEEKYSFEIGGLQTTCPDSVKIKASKSLWLQKLFLPNLTLFLDSRHF
NQSEWDRLEHFAPPFGFMELNYSLVQKVTRFPVPQQQLLLASLPAGSLRCITCAVVGNGG
ILNNSHMGQEIDSHDYVFRLSGALIKGYEQDVGTRTSFYGF TAFSLTQSLILGNRGFKNVP
LGKDVRYLHFLEGTRDYEWLEALLMNQTVMSKNLFWFRHRPQEAFREALHMDRYLLLHPDFL
RYMKNRFLRSKTL DGAHWRIYRPTTGALLLLTALQLCDQVSAYGFITEGHERFSDHYDTSW
KRLIFYINHDFKLEREVWKRLHDEGIIRLYQRP GPGTAKAKN

FIGURE 243

CGATGCGCGGACCCGGGCACCCCCTCCTCCTGGGGCTGCTGCTGGTGCTGGGGCCTTCGCCG
GAGCAGCGAGTGGAATTTGTTCCCTCGAGATCTGAGGATGAAGGACAAGTTTCTAAACACCT
TACAGGCCCTCTTTATTTTAGTCCAAAGTGCAGCAAACACTTCCATAGACTTTATCACAACA
CCAGAGACTGCACCATTCCTGCATACTATAAAAGATGCGCCAGGCTTCTTACCCGGCTGGCT
GTCAGTCCAGTGTGCATGGAGGATAAGTGAAGCAGACCGTACAGGAGCAGCACACCAGGAGCC
ATGAGAAGTGCCTTGGAACCAACAGGGAAACAGAACTATCTTTATACACATCCCCTCATGG
ACAAGAGATTTATTTTGCAGACAGACTCTCCATAAGTCCTTTGAGTTTTGTATGTTGTTG
ACAGTTTGCAGATATATATTCGATAAATCAGTGTACTTGACAGTGTTATCTGTCACTTATTT

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FIGURE 244

MRGPGHPLLLGLLLVLGPSPEQRVEIVPRDLRMKDKFLKHLTGPLYFSPKCSKHFHRLYHNT
RDCTIPAYYKRCARLLTRLAVSPVCMEDK

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FIGURE 245

GGGCTGGGCCCCGCGCAGCTCCAGCTGGCCGGCTTGGTCCTGCGGTCCCTTCTCTGGGAGG
CCCGACCCCGCGCGCCAGCCCCACCATGCCACCCGCGGGGCTCCGCCGGGCGCGCCG
CTCACCGCAATCGCTCTGTTGGTGCTGGGGGCTCCCCTGGTGCTGGCCGGCGAGGACTGCCT
GTGGTACCTGGACCGGAATGGCTCCTGGCATCCGGGGTTTAACTGCGAGTTCTTCACCTTCT
GCTGCGGGACCTGCTACCATCGGTACTGCTGCAGGGACCTGACCTTGCTTATCACCGAGAGG
CAGCAGAAGCACTGCCTGGCCTTCAGCCCCAAGACCATAGCAGGCATCGCCTCAGCTGTGAT
CCTCTTTGTTGCTGTGGTTGCCACCACCATCTGCTGCTTCCTCTGTTCTGTTGCTACCTGT
ACCGCCGGCGCCAGCAGCTCCAGAGCCCATTGAAGGCCAGGAGATTCCAATGACAGGCATC
CCAGTGACGCCAGTATACCCATACCCCCAGGACCCCCAAAGCTGGCCCTGCACCCCCACAGCC
TGGCTTCATGTACCCACCTAGTGGTCCTGCTCCCCAATATCCACTCTACCCAGCTGGGCCCC
CAGTCTACAACCCTGCAGCTCCTCCTCCCTATATGCCACCACAGCCCTCTTACCCGGGAGCC
TGAGGAACCAGCCATGTCTCTGCTGCCCCCTTCAGTGATGCCAACCTTGGGAGATGCCCTCAT
CCTGTACCTGCATCTGGTCCTGGGGGTGGCAGGAGTCCTCCAGCCACCAGGCCCCAGACCAA
GCCAAGCCCTGGGCCCTACTGGGGACAGAGCCCCAGGGAAGTGGAACAGGAGCTGAACTAGA
ACTATGAGGGGTGGGGGGAGGGCTTGGAATTATGGGCTATTTTTACTGGGGGCAAGGGAGG
GAGATGACAGCCTGGGTACAGTGCCTGTTTTCAAATAGTCCCTCTGCTCCCAAGATCCCAG
CCAGGAAGGCTGGGGCCCTACTGTTTGTCCCCTCTGGGCTGGGGTGGGGGGAGGGAGGAGGT
TCCGTCAGCAGCTGGCAGTAGCCCTCCTCTCTGGCTGCCCCACTGGCCACATCTCTGGCCTG
CTAGATTAAAGCTGTAAAGACAAAA

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FIGURE 246

MPPAGLRRAAPLTAIALLVLGAPLVLAGEDCLWYLDNRGSHWPGFNCEFFTFCCGTCYHRYC
CRDLTLLITERQQKHCLAFSPKTIAGIASAVILFVAVVATTICCFLCSCCYLYRRRQQLQSP
FEGQEIPMTGIPVQPVYPYPQDPKAGPAPPQPGFMYPPSGPAPQYPLYPAGPPVYNPAAPP
YMPPQPSYPGA

FIGURE 247

GGGGGAGCTAGGCCGGCGGCAGTGGTGGTGGCGGGCGGCGCAAGGGTGAGGGCGGCCCCAGAA
CCCCAGGTAGGTAGAGCAAGAAGATGGTGTCTTGCCCCCTCAAATGGTCCCTTGCAACCATG
TCATTTCTACTTTCCCTCACTGTTGGCTCTCTTAAGTGTGTCCACTCCTTCATGGTGTGACAG
CACTGAAGCATCTCCAAAACGTAGTGATGGGACACCATTTCCCTTGGAATAAAAATACGACITTC
CTGAGTACGTCACTCCAGTTCAATTATGATCTCTTGATCCATGCAAAACCTTACCACGCTGACC
TTCTGGGGAACCAAGTAGAAATCACAGCCAGTCAGCCCACCAGCACCATCATCCTGCA
TAGTCACCACCTGCAGATATCTAGGGCCACCCTCAGGAAGGGAGCTGGAGAGAGGCTATCGG
AAGAACCCCTGCAGGTCCTGGAACACCCCCCTCAGGAGCAAAATGCACTGCTGGCTCCCGAG
CCCCCTCCTTGTCGGGCTCCCGTACACAGTTGTCACTTCACTATGCTGGCAATCTTTCCGGAGAC
TTTCCACGGATTTTACAAAAGCACCTACAGAACCAAGGAAGGGGAACTGAGGATACTAGCAT
CAACACAATTTGAACCCACTGCAGCTAGAATGGCCTTTCCCTGCTTTGATGAACCTGCCTTC
AAAGCAAGTTTCTCAATCAAAATTAGAAGAGAGCCAAGGCACCTAGCCATCTCCAATATGCC
ATTGGTGAAATCTGTGACTGTTGCTGAAGGACTCATAGAAGACCATTTTGATGTCACTGTGA
AGATGAGCACCTATCTGGTGGCCTTCATCATTTTCAAGATTTTGAGTCTGTCAAGATAACC
AAGAGTGGAGTCAAGGTTTCTGTTTATGCTGTGCCAGACAAGATAAATCAAGCAGATTATGC
ACTGGATGCTGCGGTGACTCTTCTAGAATTTTATGAGGATTATTTCAAGCATACCGTATCCCC
TACCCAAACAGATCTTGCTGCTATTCCCGACTTTCACTCTGGTGTATGGAAAACCTGGGGA
CTGACAACATATAGAGAATCTGCTCTGTTGTTTATGATGCAGAAAAGTCTTCTGCATCAAGTAA
GCTTGGCATCACAGTGACTGTGGCCCATGAACTGGCCACCAGTGGTTTGGGAACCTGGTCA
CTATGGAATGGTGGAAATGATCTTTGGCTAAATGAAGGATTTGCCAAATTTATGGAGTTTGTG
TCTGTCAAGTGTGACCCATCCTGAACTGAAAGTTGGAGATTATTTCTTTGGCAAATGTTTTGA
CGCAATGGAGGTAGATGCTTTAAATTCCTCACACCCTGTGTCTACACCTGTGGAAAATCCTG
CTCAGATCCGGGAGATGTTTGATGATGTTTCTTATGATAAGGGAGCTTGATTCTGAATATG
CTAAGGGAGTATCTTAGCGCTGACGCATTTAAAAGTGGTATTGTACAGTATCTCCAGAAGCA
TAGCTATAAAAATACAAAAACGAGGACCTGTGGGATAGTATGGCAAGTATTTGCCCTACAG
ATGGTGTAAAAGGGATGGATGGCTTTTGCTCTAGAAGTCAACATTCATCTTCATCCTCACAT
TGGCATCAGGAAGGGGTGGATGTGAAAACCATGATGAACACTTGGACACTGCAGAGGGGTTT
TCCCCTAATAACCATCACAGTGAGGGGGAGGAATGTACACATGAAGCAAGAGCACTACATGA
AGGGCTCTGACGGCGCCCCGGACACTGGGTACCTGTGGCATGTTCCATTGACATTCATCACC
AGCAAATCCAACATGGTCCATCGATTTTGTCTAAAACAAAAACAGATGTGCTCATCCTCCC
AGAAGAGGTGGAATGGATCAAATTTAATGTGGGCATGAATGGCTATTACATTGTGCATTACG
AGGATGATGGATGGGACTCTTTGACTGGCCTTTTAAAAGGAACACACACAGCAGTCAAGCAT
AATGATCGGGCAAGTCTCATTAACAATGCATTTCAAGCTCGTCAGCATTGGGAAGCTGTCCAT
TGAAAAGGCCTTGGATTTATCCCTGTACTTGAAACATGAACTGAAATTATGCCCGTGTTC
AAGGTTTGAATGAGCTGATTCTATGTATAAGTTAATGGAGAAAAGAGATATGAATGAAGTG
GAAACTCAATTCAAGGCCTTCTCATCAGGCTGCTAAGGGACCTCATTGATAAGCAGACATG
GACAGACGAGGGCTCAGTCTCAGAGCAAATGCTGCGGAGTGAACACTACTCCTCGCCTGTG
TGCACAACTATCAGCCGTGCGTACAGAGGGCAGAAGGCTATTTCAAGAAAGTGAAGGAATCC
AATGGAACTTTGAGCCTGCCTGTGACGCTGACCTTGGCAGTGTGTTGCTGTGGGGGGCCAGAG
CACAGAAGGCTGGGATTTTCTTTATAGTAAATATCAGTTTCTTTGTCCAGTACTGAGAAAA
GCCAAATTGAATTTGCCCTCTGCAGAACCCAAAATAAGGAAAAGCTTCAATGGCTACTAGAT
GAAAGCTTTAAGGGAGATAAAATAAAAACTCAGGAGTTTCCACAAATTTCTTACACTCATTGG
CAGGAACCCAGTAGGATACCCACTGGCCTGGCAATTTCTGAGGAAAACTGGAACAACTTG
TACAAAAGTTTGAACCTGGCTCATCTTCATAGCCCATGGTAATGGGTACAACAAATCAA
TTCTCCACAAGAACACGGCTTGAAGAGGTAAAGGATTCTTCAGCTCTTTGAAAGAAAATGG
TTCTCAGCTCCGTTGTGTCCAACAGACAATTGAAACCATTGAAGAAAACATCGGTTGGATGG
ATAAGAATTTTGATAAAATCAGAGTGTGGCTGCAAAGTGAAAAGCTTGAACGTATGTAAAAA
TTCTCCTTCCCTTGGCCGGTTCTGTATCTCTAATCACCACATTTTGTGAGTGTATTTTCAA
ACTAGAGATGGCTGTTTTGGCTCCAAGTGGAGATACTTTTTTCCCTTCAACTCATTTTTTGA
CTATCCCTGTGAAAAGAATAGCTGTTAGTTTTTTCATGAATGGGCTTTTTTCATGAATGGGCTA
TCGCTACCATGTGTTTTGTTTCAACAGGTGTTGCCCTGCAACGTAAACCCCAAGTGTGGGT
TCCCTGCCACAGAAGAATAAAGTACCTTATTCTCTCAAAAAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 248

MVFLPLKWSLATMSFLLSSLLALLTVSTPSWCQSTEASPKRSDGTPFPWNKIRLPEYVIPVH
YDLLIHANLTTLTFWGTTKVEITASQPTSTIILHSHHLQISRATLRKGAGERLSEEPLOVLE
HPPQEQIALLAPEPLLVLGYPTTVIHYAGNLSETFHGFYKSTYRTKEGELRILASTQFEPTA
ARMAFPCFDEPAFKASFISIKIRREPRHLAISNMPLVKSVTVAEGLIEDHFDVTVKMSTYLVA
FIISDFESVSKITKSGVKVSVYAVPDKINQADYALDAAVTLLFEFYEDYFSIPYPLPKQDLAA
IPDFQSGAMENWGLTTYRESALLFDAEKSSASSKLGITVTVAHELAHQWFGNLVTMEWWNDL
WLNEGFAKFMEFVSVSVTHPELKVG DYFFGKCFDAMEVDALNSSHPVSTPVENPAQIREMFD
DVSYDKGACILNMLREYLSADAFKSGIVQYLQKHSYKNTKNEDLWDSMASICPTDGVKGMDG
FCSRSQHSSSSSHWHQEGVDVKTMMNTWTLQRGFPLITITVRGRNVHMKQEHYMKGSDGAPD
TGYLWHVPLTFITSKSNMVHRFLLKTKTDVLILPEEVEWIKFNVGMNGYYIVHYEDDGWDSL
TGLLKGTHTAVSSNDRASLINNAFQLV SIGKLSIEKALDLSLYLKHETEIMPVFQGLNELIP
MYKLMKCRDMNEVETQFKAFILRLRLDLIDKQTTWTDEGSVSEQMLRSELLLLACVHNYQPCV
QRAEGYFRKWKESNGNLSLPVDVTLAVFAVGAQSTEGWDFLYSKYQFSLSTEKSQIEFALC
RTQNKEKLQWLLDESFKGDKIKTQEFPPQILTLIGRNPVGYPLAWQFLRKNWNKLVQKFELGS
SSIAHVMVGGTTNQFSTRTRLEEVKGFFSSLKENGSQLRCVQQT IETIEENIGWMDKNFDKIR
VWLQSEKLERM

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FIGURE 249

CAGCCACAGACGGGTCATGAGCGCGGTATTACTGCTGGCCCTCCTGGGGTTCATCCTCCAC
TGCCAGGAGTGCAGGCGCTGCTCTGCCAGTTTGGGACAGTTCAGCATGTGTGGAAGGTGTCC
GACCTACCCCGGCAATGGACCCCTAAGAACACCAGCTGCGACAGCGGCTTGGGGTGCCAGGA
CACGTTGATGCTCATTGAGAGCGGACCCCAAGTGAGCCTGGTGCTCTCCAAGGGCTGCACGG
AGGCCAAGGACCAGGAGCCCCGCGTCACTGAGCACCGGATGGGCCCCGGCCTCTCCCTGATC
TCCTACACCTTCGTGTGCCGCCAGGAGGACTTCTGCAACAACCTCGTTAACTCCCTCCCGCT
TTGGGCCCCACAGCCCCCAGCAGACCCAGGATCCTTGAGGTGCCCAGTCTGCTTGTCTATGG
AAGGCTGTCTGGAGGGGACAACAGAAGAGATCTGCCCCAAGGGGACCACACACTGTTATGAT
GGCCTCCTCAGGCTCAGGGGAGGAGGCATCTTCTCCAATCTGAGAGTCCAGGGATGCATGCC
CCAGCCAGGTTGCAACCTGCTCAATGGGACACAGGAAATTGGGCCCCGTGGGTATGACTGAGA
ACTGCAATAGGAAAGATTTTCTGACCTGTTCATCGGGGGACCACCATTATGACACACGGAAAC
TTGGCTCAAGAACCCACTGATTGGACCACATCGAATACCGAGATGTGCGAGGTGGGGCAGGT
GTGTGAGGAGACGCTGCTGCTCATAGATGTAGGACTCACATCAACCCTGGTGGGGACAAAAG
GCTGCAGCACTGTTGGGGCTCAAAATTCCCAGAAGACCACCATCCACTCAGCCCCCTCCTGGG
GTGCTTGTGGCCTCCTATACCCACTTCTGCTCCTCGGACCTGTGCAATAGTGCCAGCAGCAG
CAGCGTTCTGCTGAACTCCCTCCCTCCTCAAGCTGCCCCCTGTCCAGGAGACCGGCAGTGTC
CTACCTGTGTGCAGCCCCCTTGGAACCTGTTCAAGTGGCTCCCCCGAATGACCTGCCCCAGG
GGCGCCACTCATTGTTATGATGGGTACATTCATCTCTCAGGAGGTGGGCTGTCCACCAAAAT
GAGCATTACAGGGCTGCGTGGCCCAACCTTCCAGCTTCTTGTGAACCACACCAGACAAATCG
GGATCTTCTCTGCGCGTGAGAAGCGTGATGTGCAGCCTCCTGCCTCTCAGCATGAGGGAGGT
GGGGCTGAGGGCCTGGAGTCTCTCACTTGGGGGGTGGGGCTGGCACTGGCCCCAGCGCTGTG
GTGGGGAGTGGTTTGCCCTTCTCTGCTAACTCTATTACCCCCACGATTCTTCACCGCTGCTGA
CCACCCACACTCAACCTCCCTCTGACCTCATAACCTAATGGCCTTGGACACCAGATTCTTTC
CCATTCTGTCCATGAATCATCTTCCCCACACACAATCATTATCTACTCACCTAACAGCA
ACACTGGGGAGAGCCTGGAGCATCCGGACTTGCCCTATGGGAGAGGGGACGCTGGAGGAGTG
GCTGCATGTATCTGATAATACAGACCCTGTCCTTTCA

FIGURE 250

MSAVLLALLGFILPLPGVQALLCQFGTVQHVKVSDLPRQWTPKNTSCDSGLGCQDTLMLI
ESGPQVSLVLSKGCTEAKDQEPRVTEHRMGPGLSLISYTFVCRQEDFCNNLVNSLPLWAPQP
PADPGSLRCPVCLSMEGCLEGTTEEICPKGTTHCYDGLLRRLRGGGIFSNLRVQGCMPPQGCN
LLNGTQEIGPVGMTENCNRKDFLTCHRGTTIMTHGNLAQEPTDWTTSNTEMCEVGQVCQETL
LLIDVGLTSTLVGTKGCSTVGAQNSQKTTIHSAPPGVLVASYTHFCSSDLCSASSSSVLLN
SLPPQAAPVPGDRQCPTCVQPLGTCSSGSPRMTCPRGATHCYDGYIHLGGGLSTKMSIQGC
VAQPSSFLLNHTRQIGIFSAREKRDVQPPASQHEGGGAEGLESLTWGVGLALAPALWWGVVCPSC

FIGURE 251

CCGACGGGCAGGACGCCCCGTTGCGCTAGCGCTGCTCAGGAGTTGGTGTCTGCTGCGCT
CAGGATGAGGGGGAATCTGGCCCTGGTGGGCGTTCTAATCAGCCTGGCCTTCCTGTCACTGCTG
CCATCTGGACATCCTCAGCCGGCTGGCGATGACGCCTGCTCTGTGCAGATCCTCGTCCCTGG
CCTCAAAGGGGATGCGGGAGAGAAGGGAGACAAAGGCGCCCCGGACGGCCTGGAAGAGTCG
GCCCCACGGGAGAAAAAGGAGACATGGGGGACAAAGGACAGAAAGGCAGTGTGGGTCTCAT
GGAAAAATTGGTCCCATTGGCTCTAAAGGTGAGAAAGGAGATTCCGGTGACATAGGACCCCC
TGGTCCTAATGGAGAACCAGGCCTCCCATGTGAGTGACGCCAGCTGCGCAAGGCCATCGGGG
AGATGGACAACCAGGTCTCTCAGCTGACCAGCGAGCTCAAGTTCATCAAGAATGCTGTGCGC
GGTGTGCGCGAGACGGAGAGCAAGATCTACCTGCTGGTGAAGGAGGAGAAGCGCTACGCGGA
CGCCCAGCTGTCTGCCAGGGCCGCGGGGGCACGCTGAGCATGCCCAAGGACGAGGCTGCCA
ATGGCCTGATGGCCGCATACCTGGCGCAAGCCGGCCTGGCCCCGTGTCTTCATCGGCATCAAC
GACCTGGAGAAGGAGGGCGCCTTCGTGTACTCTGACCACTCCCCCATGCGGACCTTCAACAA
GTGGCGCAGCGGTGAGCCCAACAATGCCTACGACGAGGAGGACTGCGTGGAGATGGTGGCCT
CGGGCGGCTGGAACGACGTGGCCTGCCACACCACCATGTACTTCATGTGTGAGTTTGACAAG
GAGAACATGTGAGCCTCAGGCTGGGGCTGCCCCATTGGGGGCCCCACATGTCCCTGCAGGGTT
GGCAGGGACAGAGCCCAGACCATGGTGCCAGCCAGGGAGCTGTCCCTCTGTGAAGGGTGGAG
GCTCACTGAGTAGAGGGCTGTTGTCTAAACTGAGAAAATGGCCTATGCTTAAGAGGAAAATG
AAAGTGTTCCTGGGGTGCTGTCTCTGAAGAAGCAGAGTTTCATTACCTGTATTGTAGCCCCA
ATGTCATTATGTAATTATTACCCAGAATTGCTCTTCCATAAAGCTTGTGCCTTTGTCCAAGC
TATACAATAAAATCTTTAAGTAGTGCAGTAGTTAAGTCCAAAAAAAAAAAAAAAAAAAAA

FIGURE 252

M R G N L A L V G V L I S L A F L S L L P S G H P Q P A G D D A C S V Q I L V P G L K G D A G E K G D K G A P G R P G R V G
P T G E K G D M G D K G Q K G S V G R H G K I G P I G S K G E K G D S G D I G P P G P N G E P G L P C E C S Q L R K A I G E
M D N Q V S Q L T S E L K F I K N A V A G V R E T E S K I Y L L V K E E K R Y A D A Q L S C Q G R G G T L S M P K D E A A N
G L M A A Y L A Q A G L A R V F I G I N D L E K E G A F V Y S D H S P M R T F N K W R S G E P N N A Y D E E D C V E M V A S
G G W N D V A C H T T M Y F M C E F D K E N M

FIGURE 253

AGTGACTGCAGCCTTCCTAGATCCCCCTCCACTCGGTTTCTCTCTTTGCAGGAGCACCGGCAG
CACCAGTGTGTGAGGGGAGCAGGCAGCGGTCTAGCCAGTTCCTTGATCCTGCCAGACCACC
CAGCCCCCGGCACAGAGCTGCTCCACAGGCACCATGAGGATCATGCTGCTATTACAGCCAT
CCTGGCCTTCAGCCTAGCTCAGAGCTTTGGGGCTGTCTGTAAGGAGCCACAGGAGGAGGTGG
TTCCTGGCGGGGGCCGCAGCAAGAGGGATCCAGATCTCTACCAGCTGCTCCAGAGACTCTTC
AAAAGCCACTCATCTCTGGAGGGATTGCTCAAAGCCCTGAGCCAGGCTAGCACAGATCCTAA
GGAATCAACATCTCCCGAGAAACGTGACATGCATGACTTCTTTGTGGGACTTATGGGCAAGA
GGAGCGTCCAGCCAGAGGGAAAGACAGGACCTTTCTTACCTTCAGTGAGGGTTCTCGGCCC
CTTCATCCCAATCAGCTTGGATCCACAGGAAAGTCTTCCCTGGGAACAGAGGAGCAGAGACC
TTTATTAGACTCTCCTACGGATGTGAATCAAGAGAACGTCCCCAGCTTTGGCATCCTCAAGT
ATCCCCCGAGAGCAGAATAGGTACTCCACTTCCGGACTCCTGGACTGCATTAGGAAGACCTC
TTTCCCTGTCCCAATCCCCAGGTGCGCACGCTCCTGTTACCCTTTCTCTTCCCTGTTCTTGT
AACATTCTTGTGCTTTGACTCCTTCTCCATCTTTTCTACCTGACCCTGGTGTGGAAACTGCA
TAGTGAATATCCCCAACCCCAATGGGCATTGACTGTAGAATACCCTAGAGTTCTGTAGTGT
CCTACATTAAAAATATAATGTCTCTCTCTATTCTCAACAATAAAGGATTTTGCATATGAA
AA

FIGURE 254

MRIMLLFTAILAFSLAQSFQAVCKEPQEEVVPGGGRSKRDPDLYQLLQRLFKSHSSLEGLLK
ALSQASTDPKESTSPEKRDMDHDFVGLMGKRSVQPEGKTGPFPLPSVRVPRPLHPNQLGSTGK
SSLGTEEQRPL

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FIGURE 255

GGGCGTCTCCGGCTGCTCCTATTGAGCTGTCTGCTCGCTGTGCCCGCTGTGCCTGCTGTGCC
CGCGCTGTGCGCGCTGCTACCGCGTCTGCTGGACGCGGGAGACGCCAGCGAGCTGGTGATTG
GAGCCCTGCGGAGAGCTCAAGCGCCCAGCTCTGCCCCAGGAGCCCAGGCTGCCCCGTGAGTC
CCATAGTTGCTGCAGGAGTGGAGCCATGAGCTGCGTCCTGGGTGGTGTATCCCCCTTGGGGC
TGCTGTTCTGCTGCGGATCCCAAGGCTACCTCCTGCCCAACGTCACTCTCTTAGAGGAG
CTGCTCAGCAAATACCAGCACAAACGAGTCTCACTCCCGGGTCCGCAGAGCCATCCCCAGGGA
GGACAAGGAGGAGATCCTCATGCTGCACAACAAGCTTCGGGGCCAGGTGCAGCCTCAGGCCT
CCAACATGGAGTACATGGTGAGCGCCGGCTCCGGCCGCAGAGGCTGGCACCGGGGGTGGGGC
CTGGGCCACCCAGCCTGCTCTGTTCCCCAGCCAGCTCTGTTCCCCAGCCAGTGCGTGTGATGG
CTGGCTCAGGGTCTCCTCTGGCAGGGGAGGATCCCGGCTCTGTTCTGTTTTGTTTGTGTTGTT
TTGAGACAGGGTCTCACTCTGCCACTGACGCTGGAGTGCAATGGCACAATCGTCATGCCCTG
AAACCTTAGACTCCCGGGGTAAAGCGATCCTGCTTCAGCCTCCCAAGTAGCTGGAACTACAG
GCATGCACCATGGTGCCCAGCTAGATTTTAAATATTTTGTGGAGATGGGGGTCTTGCTACGT
TGCCCAGGCTGGTCTTGAACTCCTAGGCTCAAGCAATCCTCCTGCCTCAGCCTCTCAAAGTG
CTAGGATTATAGGCATGAGTCACCCTGTCTGGCTCTGGCTCTGTTCTTAACATTCTGCCAAA
ACAACACACGTGGGTTCCCTGTGCAGAGCCTGCCTCGTTGCCTTCATGTCACTCTTGGTAGC
TCCACTGGGAACACAGCTCTCAGCCTTTCCACCTGGAGGCAGAGTGGGGAGGGGCCCCAGGG
CTGGGCTTTGCTGATGCTGATCTCAGCTGTGCCACACGCTAGCTGCACCACCCTGACTTCTC
CTTAGCCCCGTGTGAGCCTCACTTTCCACTTGGAGAGTCCTTCCTCGCGTGCGTGGCATGACT
GTGAGATAAGTCGAGGCTGTGAAGGGCCCGGCACAGACTGACCTGCCTCCCCAACCCCTAGG
CTTTGCTAACCGGGAAAGGAGCTAACGGTGACAGAAGACAGCCAAGGTCAACCCTCCCGGGT
GATTGTGATGGGTGTTCCAGGTGTGGTTGGGCGATGCTGCTACTTGACCCCAAGCTCCAGTG
TGGAACCTTCCTTCCTGGCTGGTTTTCCAGAACTACAGAGGAATGGACCACAGTCTTCCAGG
GTCCCTCCTCGTCCACCAACCGGGAGCCTCCACCTTGGCCATCCGTGAGCTATGAATGGCTT
TTTAAACAAACCCACGTCCCAGCCTGGGTAACATGGTAAAGCCCCGTCTCTACAAAAAAATC
CAAGTTAGCCGGGCATGGTGGTGCGCACCTGTAGTCCCAGCTGCAGTGGGACTGAGGTGGAG
GTGGAGGTGGGGGTGGGAGCTGAGGAAGGAGGATCGCTTGAGCCTGGGAAGTCGAGGCTGC
AGTGAGCTGAGATTGCACCACTGCACTCCAGCCTGGGTGACAGAGCAAGACCCTGTCTCAAAA

FIGURE 256

MSCVLGGV IPLGLLFLVCGSQGYLLPNVTLLLEELLSKYQHNEHSRVRRAIPREDKEEILML
HNKLRGQVQPQASNMEYMVSAAGSRRGWHRGWGLGHQPALFPSQLCSPASACDGLRVSSGR
GGSRLCSVLFVCFETGSHSATDAGVQWHNRHALKP

FIGURE 257

AAGGAGAGGCCACCGGGACTTCAGTGTCTCCTCCATCCCAGGAGCGCAGTGGCCACTATGGG
GTCTGGGCTGCCCCCTTGTCCTCCTCTTGACCCTCCTTGGCAGCTCACATGGAACAGGGCCGG
GTATGACTTTGCAACTGAAGCTGAAGGAGTCTTTTCTGACAAATTCCTCCTATGAGTCCAGC
TTCCTGGAATTGCTTGAAAAGCTCTGCCTCCTCCTCCATCTCCCTTCAGGGACCAGCGTCAC
CCTCCACCATGCAAGATCTCAACACCATGTTGTCTGCAACACATTGACAGCCATTGAAGCCTG
TGTCTTCTTGCCCCGGGCTTTTGGGCCGGGGATGCAGGAGGCAGGCCCCGACCCTGTCTTT
CAGCAGGCCCCCACCTCCTGAGTGGCAATAAATAAAATTCGGTATGCTG

FIGURE 258

MSGGLPLVLLLTLLGSSHGTGPGMTLQKLKESFLTNSSESSFLELLEKLCLLLHLPSGTS
VTLHHARSQHHVVCNT

FIGURE 259

AATTGTATCTGTGTAATGTTAAAAACAAACGAAATAAAATAGAAGGAAAACTTTCTGAGTTT
CAAAAAACAACAGACTAGTACTCTAAAGAACTCTTTAAAAACAATTAACTGTTAGGATTGCAGT
TATGATTGGATATTATTTAATTCTGTTTCTGATGTGGGGTTCCTCCACTGTGTTCTGTGTGC
TATTAATATTTACCATTGCAGAAGCTTCATTCACTGTTGAAAAATGAATGCTTAGTGGATCTG
TGCCTCTTACGCATATGTTACAAATTATCTGGAGTTCCTAATCAATGCAGAGTTCCCCTCCC
CTCCGATTGTTCTAAATTAATTGAAAGATGTCTGCTGTGGAAAAAGGCATGTATTTAAATCTG
TATGATTCTCAACCATCTTTAGTTGGGAAAGGTCCTTGAAAGCCAATGGAAATACTTTTTTTT
TTTTCTTGGCACTAATCAAGTGAGTGTTACCTTTTCACTTAGTAGGATGTGTTGTTACGCTA
GTAAAATAGAAACCTGTGTTTATTCTCAGGTATTTTAGAAACAACAGCCATCATTTTATTTT
ATGTGTGTGTTCTTGGCTGTATTCATAAATTATATATTTTTGGGCTATCAAATATTACTTCAT
TCAATATAAATAACAATAGTAGAAGTTGTTTACTTAGATATGCTTTCTAGTTGCATTTTCTC
AGCCTATGTAAGACTACTTTGTTGTAATAGCCTTTGAAATTTACAGTACTGTCTCTCTACTA
TCTTCAGATTACTTGATTCAAATAAACCAATTATGTTTGTAATTGATATTAATAAAACCAGA
ATAAAAGTTCATATCTACCC

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FIGURE 260

MIGYYLILFLMWGSSTVFCVLLIFTIAEASFVENECLVDLCLLRICYKLSGVPNQCRVPLP
SDCSK

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FIGURE 261

GAGGATTTGCCACAGCAGCGGATAGAGCAGGAGAGCACCACCGGAGCCCTTGAGACATCCTT
GAGAAGAGCCACAGCATAAGAGACTGCCCTGCTTGGTGTGTTTTGCAGGATGATGGTGGCCCTT
CGAGGAGCTTCTGCATTGCTGGTTCTGTTCCCTTGACAGCTTTTCTGCCCCCGCCGAGTGTAC
CCAGGACCCAGCCATGGTGCATTACATCTACCAGCGCTTTCGAGTCTTGGAGCAAGGGCTGG
AAAAATGTACCCAAGCAACGAGGGCATACATTCAAGAATTCCAAGAGTTCTCAAAAAATATA
TCTGTTCATGCTGGGAAGATGTGAGACCTACACAAAGTGAGTACAAGAGTGCAGTGGGTAACCTT
GGCACTGAGAGTTGAACGTGCCAACGGGAGATTGACTACATACAATACCTTCGAGAGGCTG
ACGAGTGCATCGTATCAGAGGACAAGACACTGGCAGAAATGTTGCTCCAAGAAGCTGAAGAA
GAGAAAAAGATCCGGACTCTGCTGAATGCAAGCTGTGACAACATGCTGATGGGCATAAAGTC
TTTGAAAATAGTGAAGAAGATGATGGACACACATGGCTCTTGGATGAAAGATGCTGTCTATA
ACTCTCCAAAGGTGTACTTATTAATTGGATCCAGAAACAACACTGTTTGGGAATTTGCAAAC
ATACGGGCATTTCATGGAGGATAACACCAAGCCAGCTCCCCGGAAGCAAATCCTAACACTTTC
CTGGCAGGGAACAGGCCAAGTGATCTACAAAGGTTTTCTATTTTTTCATAACCAAGCAACTT
CTAATGAGATAATCAAATATAACCTGCAGAAGAGGACTGTGGAAGATCGAATGCTGCTGCCA
GGAGGGGTAGGCCGAGCATTGGTTTTACCAGCACTCCCCCTCACTTACATTGACCTGGCTGT
GGATGAGCATGGGCTCTGGGCCATCCACTCTGGGCCAGGCACCCATAGCCATTTGGTTCTCA
CAAAGATTGAGCCGGGCACACTGGGAGTGGAGCATTTCATGGGATACCCCATGCAGAAGCCAG
GATGCTGAAGCCTCATTCTCTTGTGTGGGGTTCTCTATGTGGTCTACAGTACTGGGGGCCA
GGGCCCTCATCGCATCACCTGCATCTATGATCCACTGGGCACTATCAGTGAGGAGGACTTGC
CCAACTTGTTCTTCCCCAAGAGACCAAGAAGTCACTCCATGATCCATTACAACCCAGAGAT
AAGCAGCTCTATGCCTGGAATGAAGGAAACCAGATCATTTACAAACTCCAGACAAAGAGAAA
GCTGCCTCTGAAGTAATGCATTACAGCTGTGAGAAAGAGCACTGTGGCTTTGGCAGCTGTTCT
TACAGGACAGTGAGGCTATAGCCCCTTCACAAATATAGTATCCCTCTAATCACACACAGGAAG
AGTGTGTAGAAGTGGAATACGTATGCCTCCTTTCCCAAATGTCAGTGCCTTAGGTATCTTC
CAAGAGCTTAGATGAGAGCATATCATCAGGAAAGTTTCAACAATGTCCATTACTCCCCAAA
CCTCCTGGCTCTCAAGGATGACCACATTCTGATACAGCCTACTTCAAGCCTTTTGTTTTACT
GCTCCCCAGCATTTACTGTAACCTCTGCCATCTTCCCTCCCACAATTAGAGTTGTATGCCAGC
CCCTAATATTACCACTGGCTTTTCTCTCCCCTGGCCTTTGCTGAAGCTCTTCCCTCTTTTT
CAAATGTCTATTGATATTCTCCCATTTTCACTGCCCAACTAAAATACTATTAATATTTCTTT
CTTTCTTTTTCTTTTTTTTGAGACAAGGTCTCACTATGTTGCCAGGCTGGTCTCAAACCTCC
AGAGCTCAAGAGATCCTCCTGCCTCAGCCTCCTAAGTACCTGGGATTACAGGCATGTGCCAC
CACACCTGGCTTAAAATACTATTTCTTATTGAGGTTTAACCTCTATTTCCCCTAGCCCTGTC
CTTCCACTAAGCTTGGTAGATGTAATAATAAAGTGAAAATATTAACATTTGAATATCGCTTT
CCAGGTGTGGAGTGTGTCACATCATTGAATTCTCGTTTCACCTTTGTGAAACATGCACAAG
TCTTTACAGCTGTCAATTCTAGAGTTTAGGTGAGTAACACAATTACAAAGTGAAAGATACAGC
TAGAAAATACTACAAATCCCATAGTTTTTCCATTGCCCAAGGAAGCATCAAATACGTATGTT
TGTTACCTACTCTTATAGTCAATGCGTTTCATCGTTTCAGCCTAAAAATAATAGTCTGTCCC
TTTAGCCAGTTTTTCATGTCTGCACAAGACCTTTCAATAGGCCTTTCAAATGATAATTCCTCC
AGAAAACCAGTCTAAGGGTGAGGACCCCAACTCTAGCCTCCTCTGTCTTGTCTGTCTCTGT
TTCTCTCTTTCTGCTTTAAATTCAATAAAAGTGACACTGAGCAAAAAAAAAAAAAA

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FIGURE 262

MMVALRGASALLVLFLAAFLPPPQCTQDPAMVHYIYQRFVLEQGLEKCTQATRAYIQEFQE
FSKNISVMLGRCQTYTSEYKSAVGNLALRVERAQREIDYIQYLREADECIVSEDKTLAEMLL
QEAEEEKKIRTLLNASCDNMLMGIKSLKIVKKMMDTHGSWMKDAVYNPKVYLLIGSRNNTV
WEFANIRAFMEDNTKPAPRKQILTLSWQGTGQVIYKGFLFFHNQATSNEIIKYNLQKRTVED
RMLLPGGVGRALVYQHSPSTYIDLAVDEHGLWAIHSGPGTHSHLVLTKEPGTLGVEHSWDT
PCRSQDAEASFLLCGVLYVVYSTGGQGPHRITCIYDPLGTISEEDLPNLFFPKRPRSHSMIH
YNPRDKQLYAWNEGNQIIYKLQTKRKLPLK

FIGURE 263

GGGCGCCCGCTACTCACTAGCTGAGGTGGCAGTGGTTCACCAACATGGAGCTCTCGCAGA
TGTCGGAGCTCATGGGGCTGTGGGTGTGCTTGGGCTGCTGGCCCTGATGGCGACGGCGGGCG
GTAGCGCGGGGGTGGCTGCGCGCGGGGGAGGAGAGGAGCGGCCGGCCCGCCTGCCAAAAGC
AAATGGATTTCCACCTGACAAATCTTCGGGATCCAAGAAGCAGAAACAATATCAGCGGATTTC
GGAAGGAGAAGCCTCAACAACACAACCTTCACCCACCGCCTCCTGGCTGCAGCTCTGAAGAGC
CACAGCGGGAACATATCTTGATGGACTTTAGCAGCAATGGCAAATACCTGGCTACCTGTGC
AGATGATCGCACCATCCGCATCTGGAGCACCAAGGACTTCCTGCAGCGAGAGCACCGCAGCA
TGAGAGCCAACGTGGAGCTGGACCACGCCACCCTGGTGGCTTCAGCCCTGACTGCAGAGCC
TTCATCGTCTGGCTGGCCAACGGGGACACCCTCCGTGTCTTCAAGATGACCAAGCGGGAGGA
TGGGGGCTACACCTTCACAGCCACCCAGAGGACTTCCCTAAAAAGCACAAGGCGCCTGTCA
TCGACATTGGCATTGCTAACACAGGGAAGTTTATCATGACTGCCTCCAGTGACACCACTGTCT
CTCATCTGGAGCCTGAAGGGTCAAGTGCTGTCTACCATCAACACCAACCAGATGAACAACAC
ACACGCTGCTGTATCTCCCTGTGGCAGATTTGTAGCCTCGTGTGGCTTCACCCAGATGTGA
AGGTTTGGGAAGTCTGCTTTGGAAAGAAGGGGGAGTTCCAGGAGGTGGTGGCAGCCTTCGAA
CTAAAGGGCCACTCCGCGGCTGTGCACTCGTTTGCTTTCTCCAACGACTCACGGAGGATGGC
TTCTGTCTCCAAGGATGGTACATGGAACTGTGGGACACAGATGTGGAATACAAGAAGAAGC
AGGACCCCTACTTGCTGAAGACAGGCCGCTTTGAAGAGGCGGCGGTGCCGCGCCGTGCCGC
CTGGCCCTCTCCCCAACGCCACAGGTCTTGGCCTTGGCCAGTGGCAGTAGTATTCTCTCTA
CAATACCCGGCGGGGCGAGAAGGAGGAGTGCTTTGAGCGGGTCCATGGCGAGTGTATCGCCA
ACTTGTCTTTGACATCACTGGCCGCTTTCTGGCCTCCTGTGGGGACCGGGCGGTGCCGCTG
TTTCACAACACTCCTGGCCACCGAGCCATGGTGGAGGAGATGCAGGGCCACCTGAAGCGGGC
CTCCAACGAGAGCACCCGCCAGAGGCTGCAGCAGCAGCTGACCCAGGCCCAAGAGACCCTGA
AGAGCCTGGGTGCCCTGAAGAAGTGACTCTGGGAGGGCCCGGCGCAGAGGATTGAGGAGGAG
GGATCTGGCCTCCTCATGGCACTGCTGCCATCTTTCTCCAGGTGGAAGCCTTTCAGAAGG
AGTCTCCTGGTTTTCTTACTGGTGGCCCTGCTTCTTCCCATTGAACTACTCTTGTCTACTT
AGGTCTCTCTCTTCTTGTGGCTGTGACTCCTCCCTGACTAGTGGCCAAGGTGCTTTTCTTC
CTCCAGGCCCAGTGGGTGGAATCTGTCCCCACCTGGCACTGAGGAGAATGGTAGAGAGGAG
AGGAGAGAGAGAGAGAATGTGATTTTGGCCTTGTTGGCAGCACATCCTCACACCCAAAGAAG
TTTGTAATGTTCAGAACAACTAGAGAACACCTGAGTACTAAGCAGCAGTTTTGCAAGGA
TGGGAGACTGGGATAGCTTCCCATCACAGAACTGTGTTCCATCAAAAAGACACTAAGGGATT
TCCTTCTGGGCCTCAGTTCTATTTGTAAGATGGAGAATAATCCTCTCTGTGAACTCCTTGCA
AAGATGATATGAGGCTAAGAGAATATCAAGTCCCCAGGTCTGGAAGAAAAGTAGAAAAGAGT
AGTACTATTGTCCAATGTGATGAAAGTGTTAAAGTGGAACCAGTGTGCTTTGAAACCAAA
TTAGAAACACATTCCTTGGGAAGGCAAAGTTTTCTGGGACTTGATCATACATTTTATATGGT
TGGGACTTCTCTCTTCGGGAGATGATATCTTGTTTAAGGAGACCTCTTTTCAGTTCATCAAG
TTCATCAGATATTGAGTGCCCACTCTGTGCCCAAATAAATATGAGCTGGGGATTAAAAAAA
AA

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FIGURE 264

MELSQMSELMGLSVLLGLLALMATAAVARGWLRAGEERSGRPACQKANGFPPDKSSGSKKQK
QYQIRIRKEKPQHNFTHRLLAAALKSHSGNISCMDFSSNGKYLATCADDRTIRIWSTKDFLQ
REHRSMRANVELDHATLVRFPDCRAFI VWLANGDTLRVFKMTKREDGGYTFTATPEDFPPK
HKAPVIDIGIANTGKFIMTASSDTTVLIWSLKGQVLSTINTNQMNNTHAAVSPCGRFVASCG
FTPDVKVWEVCFGKKGEFQEVVRAFELKGHSAVHSFAFSNDSRRMASVSKDGTWKLWDTDV
EYKKKQDPYLLKTGRFEEAAGAAPCRLALSPNAQVLALASGSSIHLYNTRRGEKEECFERVH
GECIANLSFDITGRFLASCGDRAVRLFHNTPGHRAMVEEMQGHLKRASNESTRQRLQQQLTQ
AQETLKSLGALKK

FIGURE 265

TGGCCTCCCCAGCTTGCCAGGCACAAGGCTGAGCGGGAGGAAGCGAGAGGCATCTAAGCAGG
CAGTGTTTTGCCTTTCACCCCAAGTGACCATGAGAGGTGCCACGCGAGTCTCAATCATGCTCC
TCCTAGTAACTGTGTCTGACTGTGCTGTGATCACAGGGGCCTGTGAGCGGGATGTCCAGTGT
GGGGCAGGCACCTGCTGTGCCATCAGCCTGTGGCTTCGAGGGCTGCGGATGTGCACCCCGCT
GGGGCGGGAAGGCGAGGAGTGCCACCCCGGCAGCCACAAGGTCCCCTTCTTCAGGAAACGCA
AGCACACACCTGTCTTGTCTTGCCCAACCTGCTGTGCTCCAGGTTCCCGGACGGCAGGTAC
CGCTGCTCCATGGACTTGAAGAACATCAATTTTATAGGCGCTTGCCTGGTCTCAGGATACCCA
CCATCCTTTTCTGAGCACAGCCTGGATTTTATTTCTGCCATGAAACCCAGCTCCCATGAC
TCTCCCAGTCCCTACACTGACTACCTGATCTCTTGTCTAGTACGCACATATGCACACAG
GCAGACATACCTCCCATCATGACATGGTCCCCAGGCTGGCCTGAGGATGTCACAGCTTGAGG
CTGTGGTGTGAAAGGTGGCCAGCCTGGTTCTCTTCCCTGCTCAGGCTGCCAGAGAGGTGGTA
AATGGCAGAAAGGACATTCCCCCTCCCCTCCCAGGTGACCTGCTCTCTTTCTGGGCCCTG
CCCCCTCTCCCCACATGTATCCCTCGGTCTGAATTAGACATTCTGGGCACAGGCTCTTGGGT
GCATTGCTCAGAGTCCCAGGTCCTGGCCTGACCCTCAGGCCCTTCACGTGAGGTCTGTGAGG
ACCAATTTGTGGGTAGTTCATCTTCCCTCGATTGGTTAACTCCTTAGTTTTAGACCACAGAC
TCAAGATTGGCTCTTCCCAGAGGGCAGCAGACAGTCACCCCAAGGCAGGTGTAGGGAGCCCA
GGGAGGCCAATCAGCCCCCTGAAGACTCTGGTCCCAGTCAGCCTGTGGCTTGTGGCCTGTGA
CCTGTGACCTTCTGCCAGAATTGTCATGCCTCTGAGGCCCCCTCTTACCACACTTTACCAGT
TAACCACTGAAGCCCCCAATTTCCACAGCTTTCCATTAAATGCAAATGGTGGTGGTTCAA
TCTAATCTGATATTGACATATTAGAAGGCAATTAGGGTGTTCCTTAAACAACCTCCTTTCCA
AGGATCAGCCCTGAGAGCAGGTGGTGAATTTGAGGAGGGCAGTCCTCTGTCCAGATTGGGG
TGGGAGCAAGGGACAGGGAGCAGGGCAGGGGCTGAAAGGGGCACTGATTGAGACCAGGGAGG
CAACTACACACCAACATGCTGGCTTTAGAATAAAAGCACCAACTGAAAAA

FIGURE 266

MRGATRVSIMLLLVTVSDCAVITGACERDVQCGAGTCCAI SLWLRGLRMCTPLGREGE ECHP
GSHKVPFFRKRKHHTCPCLPNLLCSRFPDGRYRCSMDLKNINF

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FIGURE 267

AGCGCCCGGGCGTCGGGGCGGTAAAAGGCCGGCAGAAGGGAGGCACTTGAGAAATGTCCTTTC
CTCCAGGACCCAAGTTTCTTCACCATGGGGATGTGGTCCATTGGTGCAGGAGCCCTGGGGGC
TGCTGCCTTGGCATTGCTGCTTGCCAACACAGACGTGTTTCTGTCCAAGCCCCAGAAAGCGG
CCCTGGAGTACCTGGAGGATATAGACCTGAAAACACTGGAGAAGGAACCAAGGACTTTCAAA
GCAAAGGAGCTATGGGAAAAAATGGAGCTGTGATTATGGCCGTGCGGAGGCCAGGCTGTTT
CCTCTGTGAGAGGAAGCTGCGGATCTGTCCTCCCTGAAAAGCATGTTGGACCAGCTGGGCG
TCCCCCTCTATGCAGTGGTAAAGGAGCACATCAGGACTGAAGTGAAGGATTTCCAGCCTTAT
TTCAAAGGAGAAATCTTCCTGGATGAAAAGAAAAAGTTCTATGGTCCCAAAGGCGGAAGAT
GATGTTTATGGGATTTATCCGTCTGGGAGTGTGGTACAACTTCTTCCGAGCCTGGAACGGAG
GCTTCTCTGGAAACCTGGAAGGAGAAGGCTTCATCCTTGGGGGAGTTTTCGTGGTGGGATCA
GGAAAGCAGGGCATTCTTCTTGAGCACCGAGAAAAAGAATTTGGAGACAAAGTAAACCTACT
TTCTGTTCTGGAAGCTGCTAAGATGATCAAACCACAGACTTTGGCCTCAGAGAAAAAATGAT
TGTGTGAAACTGCCCAGCTCAGGGATAACCAGGGACATTACCTGTGTTTCATGGGATGTATT
GTTTCCACTCGTGTCCCTAAGGAGTGAGAAACCCATTTATACTCTACTCTCAGTATGGATTA
TTAATGTATTTTAATATTCTGTTTAGGCCCCACTAAGGCAAAATAGCCCCAAAACAAGACTGA
CAAAAATCTGAAAAACTAATGAGGATTATTAAGCTAAAACCTGGGAAATAGGAGGCTTAAAA
TTGACTGCCAGGCTGGGTGCAGTGGCTCACACCTGTAATCCCAGCACTTTGGGAGGCCAAGG
TGAGCAAGTCACTTGAGGTTCGGGAGTTTCGAGACCAGCCTGAGCAACATGGCGAAACCCGTC
TCTACTAAAAATACAAAAATCACCCGGGTGTGGTGGCAGGCACCTGTAGTCCCAGCTACCCG
GGAGGCTGAGGCAGGAGAATCACTTGAACCTGGGAGGTGGAGGTTGCGGTGAGCTGAGATCA
CACCACTGTATTCCAGCCTGGGTGACTGAGACTCTAACTAA

FIGURE 268

MSFLQDPSFFTGMWSIGAGALGAAALALLLANTDVFLSKPQKALEYLEDIDLKTLEKEPR
TFKAKELWEKNGAVIMAVRRPGCFLCREEAADLSSLKSMLDQLGVPLYAVVKEHIRTEVKDF
QPYFKGEIFLDEKKKFYGPQRRKMMFMGFIRLGWYNFFRAWNGGFSGNLEGEFGFILGGVFV
VGSGKQGILLEHREKEFGDKVNLLSVLEAAKMIKPQTLASEKK

FIGURE 269

ACGGACCGAGGGTTGAGGGAGGGACACGGACCAGGAACCTGAGCTAGGTCAAAGACGCCCCG
GGCCAGGTGCCCCGTGCGAGGTGCCCCCTGGCCGGAGATGCGGTAGGAGGGGCGAGCGCGAGA
AGCCCCCTTCCTCGGCGCTGCCAACCCGCCACCCAGCCCATGGCGAACCCCGGGCTGGGGCTG
CTTCTGGCGCTGGGCCTGCCGTTCTGCTGGCCCGCTGGGGCCGAGCCTGGGGGCAAATACA
GACCACTTCTGCAAATGAGAATAGCACTGTTTTGCCTTCATCCACCAGCTCCAGCTCCGATG
GCAACCTGCGTCCGGAAGCCATCACTGCTATCATCGTGGTCTTCTCCCTCTTGGCTGCCTTG
CTCCTGGCTGTGGGGCTGGCACTGTTGGTGCGGAAGCTTCGGGAGAAGCGGCAGACGGAGGG
CACCTACCGGCCCAGTAGCGAGGAGCAGTTCTCCCATGCAGCCGAGGCCCGGGCCCCCTCAGG
ACTCCAAGGAGACGGGTGCAGGGCTGCCTGCCCATCTAGGTCCCCTCTCCTGCATCTGTCTCC
CTTCATTGCTGTGTGACCTTGGGGAAAGGCAGTGCCCTCTCTGGGCAGTCAGATCCACCCAG
TGCTTAATAGCAGGGAAGAAGGTACTTCAAAGACTCTGCCCCCTGAGGTCAAGAGAGGATGGG
GCTATTCACTTTTATATATTTATATAAAATTAGTAGTGAGATGTAAAAAAAAAAAAAAAAAAAA

FIGURE 270

MANPGLGLLLALGLPFLLARWGRAWGQIQTTSANENSTVLPSTSSSSDGNLRPEAITAIIV
VFSLLAALLLAVGLALLVRKLREKRQTEGTYRPSSEEQFSHAAEARAPQDSKETVQGCLPI

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FIGURE 271

AATATATCATCTATTTATCATTAAATCAATAATGTATTCTTTTATTCCAATAACATTTGGGTT
TTGGGATTTTAAATTTTCAAACACAGCAGAAATGACATTTTTCTGTCACTATTATTATTGTTG
GTATGTGAAGCTATTTGGAGATCCAATTCAGGAAGCAACACATTGGAGAATGGCTACTTTCT
ATCAAGAAATAAAGAGAACCACAGTCAACCCACACAATCATCTTTAGAAGACAGTGTGACTC
CTACCAAAGCTGTCAAAACACAGGCAAGGGCATAGTTAAAGGACGGAATCTTGACTCAAGA
GGGTTAATTCTTGGTGCTGAAGCCTGGGGCAGGGGTGTAAAGAAAAACACTTAGATTCAATG
ATTGTAAATTTAAGGCAAATACACATATTAGTATTACCTTAGTGTAATGTATCCCTGTCATA
TATACAATAAGGTGAAATTATAAGTACCCTATGCAGTTGGCTGGACAGTTCTAAATTGGACT
TTATTAATTTTAAAATCAGTAACTGATTTATCACTGGCTATGTGCTTAGATCTACAGGAGA
TCATATAATTTGATACAAATAAAAGAAAAGTGTCTCTCCCCTTACAGAATTGACATTTTAA
ATGCGATACAGTTAGAATAGGAAATATGACATTAGAAAGGAAGAATGACAGGGAGAAAGGAA
AGAAGGGAAAATGTTGCCAAGGAAAAAAAAA

FIGURE 272

MTFFLSLLLLLVCEAIWRSNSGSNTLENGYFLSRNKENHSQPTQSSLEDSVTPTKAVKTTGK
GIVKGRNLDSRGLILGAEAWGRGVKKNT

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FIGURE 273

GCCAGGAATAACTAGAGAGGAAACAATGGGGTTATTTCAGAGGTTTTGTTTTCTCTTAGTTCT
GTGCCCTGCTGCACCAGTCAAATACTTCTTTCATTAAAGCTGAATAATAATGGCTTTGAAGATA
TTGTTCATTGTTTATAGATCCTAGTGTGCCAGGAAGATGAAAAAATAATTGAACAAAATAGAGGAT
ATGGTGACTACAGCTTCTACGTACCTGTTTGAAGCCACAGAAAAAGATTTTTTTCAAAAA
TGTATCTATATTAATTCCTGAGAATTGGAAGGAAAACTCTCAGTACAAAAGGCCAAAAATG
AAAACCATAAACATGCTGATGTTATAGTTGCACCACCTACACTCCAGGTAGAGATGAACCA
TACACCAAGCAGTTTACAGAATGTGGAGAGAAAGGCCAATACATTCACCTTCACCCCTGACCT
TCTACTTTGGAAAAAAACAAAATGAATATGGACCACCAGGCAAACCTGTTTGTCCATGAGTGGG
CTCACCTCCGGTGGGGAGTGTTGTATGATGATACAAATGAGATCAGCTTTTACCGTGCTAAG
TCAAAAAAATCGAAGCAACAAGGTGTTCCGCAAGGTATCTCTGGTAGAAATAGAGTTTATAG
GTGTCAAGGAGGCAGCTGTCTTAGTAGAGCATGCAGAATTGATTCTACAACAAAACCTGTATG
GAAAAGATTGTCAATTTCTTCTGATAAAGTACAAACAGAAAAAGCATCCATAATGTTTATG
CAAAGTATTGATTCTGTTGTTGAATTTTGTAAACGAAAAAACCCATAATCAAGAAGCTCCAAG
CCTACAAAAACATAAAGTGCAATTTTGAAGATACATGGGAGTGATTAGCAATTCGTAGGATT
TTAAAAACACCATAACCCATGGTGACACCACCTCTCCACCTGTCTTCTCATTTGCTGAAGATC
AGTCAAAGAATTGTGTGCTTAGTTCTTGATAAGTCTGGAAGCATGGGGGGTAAGGACCGCCT
AAATCGAATGAATCAAGCAGCAAAAACATTTCTGCTGCAGACATGTTGAAAAATGGATCCTGGG
TGGGGATGGTTCACTTTGATAGTACCTGCCACTATTGTAATAAGCTAATCCAAATAAAAAAGC
AGTGATGAAGAAACACACTCATGCGCAGGATTACCTACATATCCTCTGGGAGGAACCTCCAT
CTGCTCTGGAATTAATATGCATTTTCAAGGTGATTGGAGAGCTACATTCCCACTCGATGGAT
CCGAAGTACTGCTGCTGACTGATGGGGAGGATAACACTGCAAGTCTTGTATTGATGAAGTG
AAACAAAGTGGGGCCATTGTTTCAATTTATGCTTTGGGAAGAGCTGCTGATGAAGCAGTAAT
AGAGATGAGCAAGATAACAGGAGGAAGTCATTTTATGTTTTCAGATGAAGCTCAGAACATG
GCCTCATTGATGCTTTGGGGCTCTTACATCAGGAAATCTGATCTCTCCAGAAAGTCCCTT
CAGCTCGAAAGTAAGGGATTAACTGAAATAGTAATGCCTGGATGAACGACACTGTCTATAAT
TGATAGTACAGTGGGAAAGGACACGTTCTTCTCATCACATGGAACAGTCTGCCTCCAGTA
TTTCTCTCTGGATCCCAGTGGAAACAATAATGGAAAAATTCACAGTGGATGCAACTTCCAA
ATGGCCTATCTCAGTATTCAGGAAGTCAAGAGTGGGCACTGGGCATACAACTTCCAGCA
CAAGCGAATCCAGAAACATTAACATATTACAGTAACCTCTCGAGCAGCAAAATCTTCTGTGC
CTCCAATCACAGTGAATGCTAAAATGAATAAGGACGTAAACAGTTTCCCAGCCCAATGATT
GTTTACGCAGAAATCTACAAGGATATGTACCTGTTCTTGGAGCCAAATGTGACTGCTTTCAT
TGAATCAGAGAATGGACATACAGAAGTTTGGAACTTTGGATAATGGTGACGGCTGATT
CTTTCAAGAATGATGGAGTCTACTCCAGTATTTCACAGTATACAGAAAAATGGCAGATAT
AGCTTAAAGTTTGGGCTCATGGAGGAGCAAACTGCCAGGCTAAAATTACGGCTCCACT
GAATAGAGCCGCTACATACCAGGCTGGGTAGTGAACGGGGAAATTGAAGCAAAACCCGCCAA
GACCTGAAATTGATGAGGATACTCAGACCACCTGGAGGATTTACGCCGAACAGCATCCGGA
GGTGCTATTGTGGTATCACAAGTCCCAAGCCTTCCCTTGCCTGACCAATCCCAAGTCA
AATCACAGACCTTGATGCCACAGTTCATGAGGATAAGATTATTTACATATGGACAGCAGCAG
GAGATAATTTTGTGTTGGAAAAAGTTCAACGTTTATATCATAAGAATAAGTGCAAGTATTCTT
GATCTAAGAGACAGTTTTGTGATGCTCTTCAAGTAAATACTACTGATCTGTCCACCAAGGA
GGCCAATCCAAGGAAAGCTTTGCATTTAAACCAGAAAAATCTCAGAAGAAATGCAACCC
ACATATTTTATGCCATTAAGATATAGATAAAGCAATTTGACATCAAAGTATCCAACTT
GCACAAGTAACTTTGTTTATCCCTCAAGCAAACTCTGATGACATTGATCCTACCTACTCC
TACTCCTACTCCTACTCCTGATAAAAGTCATAATTTCTGGAGTTAATATTTCTACGCTGGTAT
TGTCTGTGATTGGGTCTGTTGTAATTGTTAACTTTATTTAAGTACCACCATTGGAACCTTA
ACGAAGAAAAAAATCTTCAAGTAGACCTAGAAGAGAGTTTTAAAAAACAAAACAATGTAAGT
AAAGGATATTTCTGAATCTTAAATTCATCCCATGTGTGATCATAACTCATAAAAAATTAAT
TTAAGATGTCGGAAGGATACTTTGATTAAATAAAAAACACTCATGGATATGAAAAAATGT
CAAGATTAAAAATTAATAGTTTCATTTATTTGTTATTTTATTTGTAAGAAATAGTGATGAAC
AAAGATCCTTTTTCATACTGATACCTGGTTGTATATTATTTGATGCAACAGTTTTCTGAAAT
GATATTTCAAAATGTCATCAAGAAATTAATATCATCTATCTGAGTAGTCAAATACAAGTAA
GGAGATGCAAAATAAACCAATTTGAAAAAATAAAAAAATAAAAAAATAAAAAAATAAAAAA
AAAAAATAAAAAAATAAAAAAATAAAAAAATAAAAAAATAAAAAAATAAAAAAATAAAAAA

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FIGURE 274

MGLFRGFVFLVLCLLHQSNTSFIKLNNNGFEDIVIVIDPSVPEDEKIIIEQIEDMVTASTY
LFEATEKRFFFKNVSILIPENWKENPQYKRPKHENHKHADVIVAPPTLPGRDEPYTKQFTEC
GEKGEYIHFTPDLLLGKKQNEYGPPGKLFVHEWAHLRWGVFDEYNEDQPFYRAKSKKIEATR
CSAGISGRNRVYKCQGGSCLSRACRIDSTTKLYGKDCQFFPDKVQTEKASIMFMQSIDSVVE
FCNEKTHNQEAPSLQNIKCNFRSTWEVISNSEDFKNTIPMVTPPPPPVFSLLKISQRIVCLV
LDKSGSMGGKDRNLNRMNQAAKHFLQTVENGSWVGMVHFDSTATIVNKLIQIKSSDERNTLM
AGLPTYPLGGTSICSGIKYAFQVIGELHSQLDGSEVLLLLTDGEDNTASSCIDEVKQSGAIVH
FIALGRAADEAVIEMSKITGGSHFYVSDEAQNNGLIDAFGALTSGNTDLSQKSLQLESKGLT
LNSNAWMNDTVIIDSTVGKDTFFLITWNSLPPSISLWDPSGTIMENFTVDATSKMAYLSIPG
TAKVGTWAYNLQAKANPETLTITVTSRAANSSVPPITVNAKMNKDVNSFPSPMIVYAEILQG
YVPVLGANVTAFIESQNGHTEVLELLDNGAGADSFKNDBGVYSRYFTAYTENGRYSLKVRAHG
GANTARLKLRPPLNRAAYIPGWVVNGEIEANPPRPEIDEDTQTTLEDFSRASGGAFVVSQV
PSLPLPDQYPPSQITDL DATVHEDKIILTWTPGDNFDVGKVQRYIIRISASILDLRDSFDD
ALQVNTTDLSPKEANSKESFAFKPENISEENATHIFIAIKSIDKSNLTSKVSANIAQVTLFIP
QANPDDIDPTPTPTPTPTPKSHNSGVNISTLVLSVIGSVVIVNFILSTTI

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FIGURE 275

CTCCTTAGGTGGAAACCCTGGGAGTAGAGTACTGACAGCAAAGACCGGAAAAGACCATACGTCCCCGG
GCAGGGGTGACAACAGGTGTCTATCTTTTGTATCTCGTGTGTGGCI GCCTTCCTATTTCAAGGAAAAGAC
GCCAAGGTAATTTTGACCCAGAGGAGCAATGATGTAGCCACCTCCFAACCTTCCCTTCTTGAACCCCC
AGTTATGCCAGGATTTACTAGAGAGTGTCAACTCAACCAGCAAGCGGCTCCTTCGGCTTAACCTTGTGG
TTGGAGGAGAGAACCTTTGTGGGGCTGCGTTCTCTTAGCAGTGTCTCAGAAGTGAAGTGCCTGAGGGTG
GACCAGAAGAAAAGGAAAGGTCCCTCTTGCTGTGGCTGCACATCAGGAAGGCTGTGATGGGAATGAA
GGTGAAGAACTTGGAGATTTCACTTCAGTCATTGCTTCTGCCTGCAAGATCATCTTTAAAAGTAGAGA
AGCTGCTCTGTGTGGTGGTTAACTCCAAGAGGCGAAGCTCGTTCTAGAAGGAAATGGATGCAAGCAGC
TCCGGGGGGCCCCAAACGCATGCTTCTGTGGTCTAGCCAGGGAAGCCCTTCCGTGGGGGGCCCCGGCT
TTGAGGGATGCCACCGGTTCTGGACGCATGGCTGATTCTGAAATGATGATGGTTGCGCCGGGGGCTGCT
TGCGTGGATTTCCCGGGTGGTGGTTTTGCTGGTGTCTCTCTGCTGTGCTATCTCTGTCTGTACATGT
TGGCTGACCCCCAAAAGGTGACGAGGAGCAGCTGGCACTGCCAGGGCCAACAGCCCCACGGGGAAG
GAGGGGTACCAGGCCGTCTTTCAGGAGTGGGAGGAGCAGCACCAGCAACTACGTGAGCAGCTGAAGCG
GCAGATCGCACAGCTCAAGGAGGAGCTGCAGGAGAGGAGTGAGCAGCTCAGGAATGGGCAGTACCAAG
CCAGCGATGCTGCTGGCCTGGGTCTGGACAGGAGCCCCCAGAGAAAACCCAGGCCGACCTCTGGCC
TTCTGCACTCGCAGGTGGACAAGGCAGAGGTGAATGCTGGCGTCAAGCTGGCCACAGAGTATGCAGC
AGTGCTTTTCGATAGCTTTACTCTACAGAAGGTGTACAGCTGGAGACTGGCCTTACCCGCCACCCCG
AGGAGAAGCCCTGTGAGGAAGGACAAGCGGGATGAGTTGGTGAAGCCATTGAATCAGCCTTGGAGACC
CTGAACAATCCTGCAGAGAACAGCCCCAATCACCGTCTTACACGGCCTCTGATTTTATAGAAGGGAT
CTACCGAACAGAAAGGGACAAAGGGACATTGTATGAGCTCACCTTCAAAGGGGACCACAAACAGCAAT
TCAAACGGCTCATCTTATTTTCGACCATTCAGCCCCATCATGAAAGTGAAAAATGAAAGCTCAACATG
GCCAACACGCTTATCAATGTTATCGTGCTCTAGCAAAAAGGGTGGACAAGTTCCGGCAGTTCATGCA
GAATTTTCAGGGAGATGTGCATTGAGCAGGATGGGAGAGTCCATCTCACTGTTGTTTACTTTGGGAAAG
AAGAAATAAATGAAGTCAAAGGAATACTTGAAAACACTTCCAAAGCTGCCAACTTCAGGAACCTTTACC
TTCATCCAGCTGAATGGAGAATTTTCTCGGGGAAAGGGACTTGATGTTGGAGCCCGCTTCTGGAAGGG
AAGCAACGTCCTTCTCTTTTCTGTGATGTGGACATCTACTTCACATCTGAATTCCTCAATACGTGTA
GGCTGAATACACAGCCAGGGAAGAAGGTATTTTATCCAGTCTTTTTCAGTCAGTACAATCCTGGCATA
ATATACGGCCACCATGATGCAGTCCCTCCCTTGGAACAGCAGCTGGTCATAAAGAAGGAACTGGATT
TTGGAGAGACTTTGGATTTGGGATGACGTGTCACTATCGGTGAGACTTCAATATAGGTGGGTTTG
ATCTGGACATCAAAGGCTGGGGCGGAGAGGATGTGCACCTTTATCGCAAGTATCTCCACAGCAACCTC
ATAGTGGTACGGACGCTGTGCGAGGACTCTTCCACCTTGGCATGAGAAGCGCTGCATGGACGAGCT
GACCCCGGAGCAGTACAAGATGTGCATGCAGTCCAAGGCCATGAACGAGGCATCCACGGCCAGCTGG
GCATGCTGGTGTTCAGGCACGAGATAGAGGCTCACCTTCGCAAAACAGAAACAGAAAGACAAGTAGCAAA
AAAACAGTAACTCCCAGAGAAGGATTGTGGGAGACACTTTTTCTTTCTTTTTCGAATTACTGAAAGTG
GCTGCAACAGAGAAAAGACTTCCATAAAGGACGACAAAAGAAATTGGACTGATGGGTGAGAGATGAGAA
AGCCTCCGATTTCTCTCTGTTGGGCTTTTTTACAACAGAAATCAAATCTCCGCTTTGCTGCAAAAGT
AACCACAGTTGCACCCCTGTGAAGTGTCTGACAAAGGCAGAATGCTTGTGAGATTATAAGCCTAATGGTG
TGGAGGTTTTGATGGTGTTTACAATACACTGAGACCTGTTGTTTTGTGTGCTCATTGAAATATTCTATG
ATTTAAGAGCAGTTTTTGTAAAAAATTCATTAGCATGAAAGGCAAGCATATTTCTCCTCATATGAATGA
GCCTATCAGCAGGGCTCTAGTTTCTAGGAATGCTAAAATATCAGAAGGCAGGAGAGGATAGGCTTA
TTATGATACTAGTAGTACATTAAGTAAATAAAATGGACCAGAAAAGAAAAGAAACCATAAATATCG
TGTCATATTTTCCCCAAGATTAAACCAAAATAATCTGCTTATCTTTTTTGGTTGTCCTTTTAACTGTCT
CCGTTTTTTTCTTTTATTTAAAAATGCACCTTTTTTCCCTTGTGAGTTATAGTCTGCTTATTTAATTA
CCACTTTGCAAGCCTTACAAGAGAGCACAAGTTGGCCTACATTTTTATATTTTTTAAGAAGATACTTT
GAGATGCATTATGAGAACTTTCAGTTCAAAGCATCAAATTGATGCCATATCCAAGGACATGCCAAATG
CTGATTTCTGTGAGGCACTGAATGTGAGGCACTGAGACATAGGGAAGGAATGTTTGTACTAATACAGA
CGTACAGATACTTTCTCTGAAGAGTATTTTGAAGAGGAGCAACTGAACACTGGAGGAAAAGAAAATG
ACACTTTCTGCTTTACAGAAAAGGAACTCATTGAGACTGGTGATATCGTGATGTACCTAAAAGTCAG
AAACCACATTTTCTCCTCAGAAGTAGGGACCGCTTTCTTACCTGTTTAAATAAACCAAAAGTATACCGT
GTGAACCAACAATCTCTTTTCAAAACAGGGTCTCCTCCTGGCTTCTGGCTTCCATAAGAAGAAATG
GAGAAAAATATATATATATATATATATATTTGTGAAAGATCAATCCATCTGCCAGAATCTAGTGGGATG
GAAGTTTTTGTCTACATGTTATCCACCCAGGCCAGGTGGAAGTAAGTGAATTTTAAATTAAGC
AGTTCTACTCAATCACCAAGATGCTTCTGAAAATTGCATTTTATTACCAATTCAAACTATTTTTTAA
AATAAATACAGTTAACATAGAGTGGTTTTCTTATTGATGAAAATTATTAGCCAGCACCAGATGCAT
GAGCTAATATCTCTTTGAGTCTTGTCTTCTGTTTGTCTCACAGTAACTCATTGTTTAAAGCTTCAA
GAACATTCAGCTGTTGGTGTGTTAAAAATGCATTGTATTGATTTGTACTGGTAGTTTATGAAATTT
AATTAACACAGGCCATGAATGGAAGGTGGTATTGACAGCTAATAAATATGATTTGTGGATATGAA

FIGURE 276

MMVRRGLLAWISRVVLLVLLCCAISVLYMLACTPKGDEEQALPRANSPTGKEGYQAVLQ
EWEEQHRNYVSSLKRQIAQLKEELQERSEQLRNGQYQASDAAGLGLDRSPPEKTQADLLAFL
HSQVDKAEVNAGVKLATEYAAVPFDSFTLQKVYQLETGLTRHPEEKPV RKDKRDELVEAIES
ALETNNPAENSPNHRPYTASDFIEGIYRTERDKGTLYELTFKGDHKHEFKRLILFRPFSP
MKVKNEKLN MANTLINVI VPLAKRVDKFRQFMQNFREMCIEQDGRVHLTVVYFGKEEINEVK
GILENTSKAANFRNFTFIQLNGEFSRGKGLDVGARFWKGSNVLLFFCDVDIYFTSEFLNTR
LNTQPGKKVFYPVLF SQYNPGIIYGHHD AVPPLEQQLVIKKETGFWRDFGFGMT CQYRSDFI
NIGGFDDL DIKGWGGEDVHLYRKYLHSNLIVVRTPV RGLFHLWHEKRCMD ELTPEQYKMCMQS
KAMNEASHGQLGMLVFRHEIEAHLRKQKQKTSSKKT

FIGURE 277

GAAAGAATGTTGTGGCTGCTCTTTTTCTGGTGACTGCCATTCATGCTGAACTCTGTCAACC
AGGTGCAGAAAATGCTTTTAAAGTGAGACTTAGTATCAGAACAGCTCTGGGAGATAAAGCAT
ATGCCTGGGATACCAATGAAGAATACCTCTTCAAAGCGATGGTAGCTTTCTCCATGAGAAAA
GTTCCCAACAGAGAAGCAACAGAAATTTCCCATGTCCTACTTTGCAATGTAACCCAGAGGGT
ATCATTCTGGTTTGTGGTTACAGACCCCTTCAAAAAATCACACCCTTCCTGCTGTTGAGGTGC
AATCAGCCATAAGAATGAACAAGAACCGGATCAACAATGCCTTCTTTCTAAATGACCAACT
CTGGAATTTTAAAAATCCCTTCCACACTTGCACCACCCATGGACCCATCTGTGCCCATCTG
GATTATTATATTTGGTGTGATATTTTGCATCATCATAGTTGCAATTGCCTACTGATTTTAT
CAGGGATCTGGCAACGTAGAAGAAAGAACAAAGAACCATCTGAAGTGGATGACGCTGAAGAT
AAGTGTGAAAACATGATCACAATTGAAATGGCATCCCTCTGATCCCCTGGACATGAAGGG
GGGCATATTAATGATGCCTTCATGACAGAGGATGAGAGGCTCACCCTCTCTGAAGGGCTGT
TGTTCTGCTTCCTCAAGAAATTAAACATTTGTTTCTGTGTGACTGCTGAGCATCCTGAAATA
CCAAGAGCAGATCATATATTTTGTTCACCATTCTTCTTTTGTAAATAAATTTTGAATGTGCT
TGAAAGTGAAAAGCAATCAATTATACCCACCAACACCACTGAAATCATAAGCTATTCACGAC
TCAAAATATTCTAAAATATTTTCTGACAGTATAGTGTATAAATGTGGTCATGTGGTATTTG
TAGTTATTGATTTAAGCATTTTGTAGAAATAAGATCAGGCATATGTATATATTTTACACTTC
AAAGACCTAAGGAAAAATAAATTTTCCAGTGGAGAATACATATAATATGGTGTAGAAATCAT
TGAAAATGGATCCTTTTTTGACGATCACTTATATCACTCTGTATATGACTAAGTAAACAAAAG
TGAGAAGTAATTATTGTAAATGGATGGATAAAAAATGGAATTACTCATATACAGGGTGGAATT
TTATCCTGTTATCACACCAACAGTTGATTATATATTTTCTGAATATCAGCCCCTAATAGGAC
AATTCTATTTGTTGACCATTTCTACAATTTGTAAAAGTCCAATCTGTGCTAACTTAATAAAG
TAATAATCATCTCTTTTTAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 278

MLWLLFFLVTAIHAE LCQPGAENAFKVRLSIRTALGDKAYAWDTNEEYLFKAMVAFSMRKVP
NREATEISHVLLCNVTQRVSFVFWVTDPSKNHTLPAVEVQSAIRMNKNRINNAFFLNDQTLE
FLKIPSTLAPPMDPSVPIWIIIFGVIFCIIIVAIALLILSGIWQRRRKNKEPSEVDDAEDKC
ENMITIENGIPSDPLDMKGGILMMPS

FIGURE 279

AACTCAAACCTCTCTCTCTGGGAAAACGCGGTGCTTGCTCCTCCCGGAGTGGCCTTGGCAGG
GTGTTGGAGCCCTCGGTCTGCCCCGTCCGGTCTCTGGGGCCAAGGCTGGGTTTCCCTCATGT
ATGGCAAGAGCTCTACTCGTGCGGTGCTTCTTCTCCTTGGCATAACAGCTCACAGCTCTTTGG
CCTATAGCAGCTGTGGAAATTTATACCTCCCGGGTGCTGGAGGCTGTTAATGGGACAGATGC
TCGGTTAAAATGCACTTTCTCCAGCTTTGCCCCGTGGGTGATGCTCTAACAGTGACCTGGA
ATTTTCGTCCTCTAGACGGGGGACCTGAGCAGTTTGTATTCTACTACCACATAGATCCCTTC
CAACCCATGAGTGGGCGGTTTAAGGACCGGTGTCTTGGGATGGGAATCCTGAGCGGTACGA
TGCCTCCATCCTTCTCTGGAAACTGCAGTTCGACGACAATGGGACATACACCTGCCAGGTGA
AGAACCCACCTGATGTTGATGGGGTGATAGGGGAGATCCGGCTCAGCGTCGTGCACACTGTA
CGCTTCTCTGAGATCCACTTCCTGGCTCTGGCCATTGGCTCTGCCTGTGCACTGATGATCAT
AATAGTAATTGTAGTGGTCCTCTTCCAGCATTACCGGAAAAAGCGATGGGCCGAAAGAGCTC
ATAAAGTGGTGGAGATAAAATCAAAAGAAGAGGAAAGGCTCAACCAAGAGAAAAAGGTCTCT
GTTTATTTAGAAGACACAGACTAAACAATTTTAGATGGAAGCTGAGATGATTTCCAAGAACAA
GAACCCTAGTATTTCTTGAAGTTAATGGAACTTTTCTTTGGCTTTTCCAGTTGTGACCCGT
TTTCCAACCAGTTCTGCAGCATATTAGATTCTAGACAAGCAACACCCCTCTGGAGCCAGCAC
AGTGCTCCTCCATATCACCAGTCATACACAGCCTCATTATTAAGGTCTTATTTAATTTCAGA
GTGTAAATTTTTTCAAGTGCTCATTAGGTTTTATAAACAAGAAGCTACATTTTTTGCCTTAA
GACACTACTTACAGTGTTATGACTTGTATACACATATATTGGTATCAAAGGGGATAAAAGCC
AATTTGTCTGTTACATTTCTTTTCACGTATTTCTTTTAGCAGCACTTCTGCTACTAAAGTTA
ATGTGTTTACTCTCTTTCCTTCCCACATTCTCAATTAAAAGGTGAGCTAAGCCTCCTCGGTG
TTTCTGATTAACAGTAAATCCTAAATTCAAACGTGTTAAATGACATTTTTATTTTTATGTCTC
TCCTTAACTATGAGACACATCTTGTTTTACTGAATTTCTTTCAATATTCCAGGTGATAGATT
TTTGTCG

FIGURE 280

MYGKSSTRAVLLLLLGIQLTALWPAAVEIYTSRVLEAVNGTDARLKCTFSSFAPVGDALTVT
WNFRPLDGGPEQFVFYYHIDPFQPMSGFRFKDRVSWDGNPERYDASILLWKLQFDDNGTYTCQ
VKNPPDVDGVIGEIRLSVVHTVRFSEIHFLALAIGSACALMIIIVIVVVL FQHYRKKRWAER
AHKVVEIKSKEEERLNQEKKVSVYLEDTD

FIGURE 281

GCATTTTTGTCTGTGCTCCCTGATCTTCAGGTCACCACCATGAAGTTCTTAGCAGTCCTGGT
ACTCTTGGGAGTTTCCATCTTTCTGGTCTCTGCCCAGAATCCGACAACAGCTGCTCCAGCTG
ACACGTATCCAGCTACTGGTCCTGCTGATGATGAAGCCCCTGATGCTGAAACCACTGCTGCT
GCAACCACTGCGACCACTGCTGCTCCTACCACTGCAACCACCGCTGCTTCTACCACTGCTCG
TAAAGACATTCCAGTTTTACCCAAATGGGTGGGGATCTCCCGAATGGTAGAGTGTGTCCCT
GAGATGGAATCAGCTTGAGTCTTCTGCAATTGGTCACAACTATTCATGCTTCCTGTGATTTC
ATCCAAC TACTTACCTTGCCTACGATATCCCCTTTATCTCTAATCAGTTTATTTCTTTCAA
ATAAAAAATAACTATGAGCAACATAAAAAAAAAAAAAA

FIGURE 282

MKFLAVLVLLGVSIFLVSAQNPTTAAPADTYPATGPADDEAPDAETTAAATTATTAAPTAT
TAASTTARKDIPVLPKWVGDLPNGRVCP

FIGURE 283

GGACTCTGAAGGTCCCAAGCAGCTGCTGAGGCCCCCAAGGAAGTGGTTCCAACCTTGGACCC
CTAGGGGTCTGGATTTGCTGGTTAACAAGATAACCTGAGGGCAGGACCCCATAGGGGAATGC
TACCTCCTGCCCTTCCACCTGCCCTGGTGTTCACGGTGGCCTGGTCCCTCCTTGCCGAGAGA
GTGTCCTGGGTGAGGACGACAGAGGACGCTCACAGACTCCAGCCCTTTGTTACCGAGAGGAC
ACTTGGCAAGGTCCAGCGATGGTCCGGAGTCCACACACAGACTGGCGGCAGGGCAGGAGGGG
GACAGTTCCTGTTGTGCTTGGTTGGACAGTAAGAGGGTCTTGGCCAGTCCAGGGTGGGGGGCG
GCAAACCTCCATAAAGAACCAGAGGGTCTGGGCCCCGGCCACAGAGTCATCTGCCCAGCTCCT
CTGCTGCTGGCCAGTGGGAGTGGCACGAGGTGGGGCTTTGTGCCAGTAAACCACAGGCTGG
ATTTGCCTGCGGGCCATGGTCCCTGTCTAGGGCAGCAATTCTCAACCTTCTTGCTCTCAGGA
CCCCAAAGAGCTTTCATTGTATCTATTGATTTTTTACCACATTAGCAATTAAAACTGAGAAAT
GGGCCGGGCACGGTGGCTCACGCCTGTAATCCCAGCACTTTGGGAGGCCGAGGCGGGTGGAT
CACCTGAGATCAGGAGTTCAAGACCAGCCTGGCCAACATGGTGAAACCTTGTCTACTAAAAA
TACAAAAAATTAGCCAGGCACAGTGGTGTGCACTGGTAGTCCCAGTTACTCGGGAGGCTGAG
GCAGGAAAATCGCTTGAACCCAGGAGGCGGACGTTGCGGTGAGCCGAGATCGCGCCGCTGAT
TCCAGCCTGGGCGACAAGAGTGAGACTCCATCTCACACA

FIGURE 284

MLPPALPPALVFTVAWSLLAERVSWVRDAEDAHRLQPFVTERTLGKVQRWSGVHTQTGGRAG
GGQFCCAWLDSKRVLASPGWGAANSIKNQRVWAPATESSAQLLCCWPVGVARGGALCQ

FIGURE 285

GTCATGCCAGTGCCTGCTCTGTGCCTGCTCTGGGCCCTGGCAATGGTGACCCGGCCTGCCTCA
GCGGCCCCCATGGGCGGCCCAGAACTGGCACAGCATGAGGAGCTGACCCTGCTCTTCCATGG
GACCCTGCAGCTGGGCCAGGCCCTCAACGGTGTGTACAGGACCACGGAGGGACGGCTGACAA
AGGCCAGGAACAGCCTGGGTCTCTATGGCCGCACAATAGAACTCCTGGGGCAGGAGGTGAGC
CGGGGCCGGGATGCAGCCAGGAACTTCGGGCAAGCCTGTTGGAGACTCAGATGGAGGAGGA
TATTCTGCAGCTGCAGGCAGAGGCCACAGCTGAGGTGCTGGGGGAGGTGGCCCAGGCACAGA
AGGTGCTACGGGACAGCGTGCAGCGGCTAGAAGTCCAGCTGAGGAGCGCCTGGCTGGGCCCT
GCCTACCGAGAAATTTGAGGTCTTAAAGGCTCACGCTGACAAGCAGAGCCACATCCTATGGGC
CCTCACAGGCCACGTGCAGCGGCAGAGGCGGGAGATGGTGGCACAGCAGCATCGGCTGCGAC
AGATCCAGGAGAGACTCCACACAGCGGCGCTCCCAGCCTGAATCTGCCTGGATGGAACTGAG
GACCAATCATGCTGCAAGGAACACTTCCACGCCCCGTGAGGCCCTGTGCAGGGAGGAGCTG
CCTGTTCACTGGGATCAGCCAGGGCGCCGGGCCCCACTTCTGAGCACAGAGCAGAGACAGAC
GCAGGCGGGGACAAAGGCAGAGGATGTAGCCCCATTGGGGAGGGGTGGAGGAAGGACATGTA
CCCTTTCATGCCTACACCCCCCTATTAAAGCAGAGTCGTGGCATTTCAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 286

MPVPALCLLWALAMVTRPASAAPMGGPELAQHEELTLLFHGTLQLGQALNGVYRTTEGRLTK
ARNSLGLYGRTIELLGQEVSRGRDAAQELRASLLETQMEEDILQLQAEATAEVLGEVAQAQK
VLRDSVQRLEVQLRSAWLGPAYREFEVLKAHADKQSHILWALTGHVQRQRREMVAAQQRRLRQ
IQERLHTAALPA

FIGURE 287

GGCAACATGGCTCAGCAGGCTTGCCCCAGAGCCATGGCAAAGAATGGACTTGTAATTTGCAT
CCTGGTGATCACCTTACTCTGGACCAGACCACCAGCCACACATCCAGATTAAAAGCCAGGA
AGCACAGCAAACGTCGAGTGAGAGACAAGGATGGAGATCTGAAGACTCAAATTGAAAAGCTC
TGGACAGAAGTCAATGCCTTGAAGGAAATTCAAGCCCTGCAGACAGTCTGTCTCCGAGGCAC
TAAAGTTCACAAGAAATGCTACCTTGCTTCAGAAGGTTTGAAGCATTTCCATGAGGCCAATG
AAGACTGCATTTCCAAAAGGAGGAATCCTGGTTATCCCCAGGAACTCCGACGAAATCAACGCC
CTCCAAGACTATGGTAAAAGGAGCCTGCCAGGTGTCAATGACTTTTGGCTGGGCATCAATGA
CATGGTCACGGAAGGCAAGTTTGTGACGTCAACGGAATCGCTATCTCCTTCTCAACTGGG
ACCGTGACAGCCTAACGGTGGCAAGCGAGAAAACTGTGTCTGTCTCCCAATCAGCTCAG
GGCAAGTGGAGTGATGAGGCCTGTCGCAGCAGCAAGAGATACATATGCGAGTTCACCATCCC
TAAATAGGTCTTTCTCCAATGTGCTCTCCAAGCAAGATTCATCATAACTTATAGGTTTCATGA
TCTCTAAGATCAAGTAAAAATCATAATTTTTTACTTTATTAATAAAATTGCAACACAAGATCAAT
GTCCATAGCAATATGATAGCATCAGCCAATTTTGCTAACACATTTCTTTGGGATTTTGCCCT
TCCTGGGGTATAGGGGATCAGAAATATTGATCCATGTGCACGCAGATAAAATGGCTTCTGCT
AAACAGACTAAAATCTTTCTCTTAGTCTTTCTCACTTGTACAAACCCAGTTTGTTTTCAA
AAATCACAGTAGCAATGCAACTCATCACTCTAGAAAAGCAAGCTTAGGCTACCTGAAAGATT
TTCCCTTGGAAGTTTAGCGTATGTTTGACTAACAAAAATCCCTACATCAGAGACTCTAGGT
GCTATATAATCCAAAACTTTTCAGCCTGTGCTCATTCTGTCCCATGCTGGCAATAATACC
TTGTGAGCCCATTAACCTTATTTTGAATTGCTCCATCTCCTGGTGGGACTTGTATCTTGTCT
GCCATATCAGAACACAAACCCCTGAAGAGGTTCTGATTTGATTTTTTTTTTTTCTTCATGCC
TACCCTTTTTTTTGGAAGTTTCCAGCCGCAATTTGAAATGAAATGACAAGGTGTATATTGAT
CAATTTTCATTCCCACCATTCGATTACAACCTCTAACTTAAATGGGTAAACCTAAGGCATAT
CAAAGAAGCAGATTGCATGATAAACGGAAATAGAAAAAAGAACCTACATTTATTTTGCTTT
AGCATCCTTACTCTCACCTTTTATGAGATTGAGAGTGGACTTACATTTCTTTTACATTT
TCGTATATTTATTTTTTTTAGCCATCATTATATGTTTAAGTCTATTATGGGCAACCAATCTT
TGGAAGCTGAAAAGTGAATTTAAAGAATGCTATCTTGAAAAATTGCATACGTCTGTGCAATT
TTTTATTCTGCCTAGTGCTATTCTGCTTGTTTAACTAGATTGTACAAAATAACTTCATTGCT
TAATATCAAATTACAAAGTTTAGACTTGGAGGAAATGGGCTTTTGTAGAAGCAAACAATTTT
AAATATATTTTGTCTTCAAATAAATAGTGTTTAAACATTGAATGTGTTTTGTGAACAATAT
CCCCTTTGCAAACCTTAACTACACATGCTTGGAATTAAGTTTTAGCTGTTTTTCATTGCTCA
ATAATAAAGCCTGAATTCTGATCAATAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

FIGURE 288

MAQQACPRAMAKNGLVICILVITLLLDQTTSHTSRLKARKHSKRRVRDKDGLKTQIEKLWT
EVNALKEIQALQTVCLRGTKVHKKCYLASEGLKHFHEANEDCISKGGILVIPRNSDEINALQ
DYGKRSLPGVNDFWLGINDMVTEGKFVDVNGIAISFLNWDRAQPNGGKRENCVLFSQSAQ GK
WSDEACRSSKRYICEFTIPK

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FIGURE 289

GCGAGGACCGGGTATAAGAAGCCTCGTGGCCTTGCCCGGGCAGCCGCAGGTTCCCCGCGCGC
CCCCGAGCCCCCGCGCCATGAAGCTCGCCGCCCTCCTGGGGCTCTGCGTGGCCCTGTCCTGCA
GCTCCGCTGCTGCTTTCTTAGTGGGCTCGGCCAAGCCTGTGGCCCAGCCTGTGCTGCGCTG
GAGTCGGCGGCGGAGGCCGGGGCCGGGACCCTGGCCAACCCCCCTCGGCACCCCTCAACCCGCT
GAAGCTCCTGCTGAGCAGCCTGGGCATCCCCGTGAACACCTCATAGAGGGCTCCCAGAAAGT
GTGTGGCTGAGCTGGGTCCCCAGGCCGTGGGGGCCGTGAAGGCCCTGAAGGCCCTGCTGGGG
GCCCTGACAGTGTTTGGCTGAGCCGAGACTGGAGCATCTACACCTGAGGACAAGACGCTGCC
CACCCGCGAGGGCTGAAAACCCCGCCGCGGGGAGGACCGTCCATCCCCTTCCCCCGGCCCT
CTCAATAAACGTGGTTAAGAGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAA

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FIGURE 290

MKLAALLGLCVALSCSSAAAFVGSAPVAPVAALESAAEAGAGTLANPLGTINPLKLLLS
SLGIPVNHLEGSQKCVNELGPQAVGAVKALKALLGALTVFG

FIGURE 291

TGAAGGACTTTTCCAGGACCCAAGGCCACACACTGGAAGTCTTGCAGCTGAAGGGAGGCACT
CCTTGGCCTCCGCAGCCGATCACATGAAGGTGGTGCCAAGTCTCCTGCTCTCCGTCCTCCTG
GCACAGGTGTGGCTGGTACCCGGCTTGGCCCCCAGTCTCAGTCGCCAGAGACCCCAGCCCC
TCAGAACCAGACCAGCAGGGTAGTGCAGGCTCCCAGGGAGGAAGAGGAAGATGAGCAGGAGG
CCAGCGAGGAGAAGGCCGGTGAGGAAGAGAAAGCCTGGCTGATGGCCAGCAGGCAGCAGCTT
GCCAAGGAGACTTCAAACCTTCGGATTTCAGCCTGCTGCGAAAGATCTCCATGAGGCACGATGG
CAACATGGTCTTCTCTCCATTTGGCATGTCTTGGCCATGACAGGCTTGATGCTGGGGGCCA
CAGGGCCGACTGAAACCCAGATCAAGAGAGGGGCTCCACTTGCAGGCCCTGAAGCCCACCAAG
CCCGGGCTCCTGCCTTCCCTCTTTAAGGGACTCAGAGAGACCCCTCTCCCGCAACCTGGAAC
GGGCCTCTCACAGGGGAGTTTTGCCTTCATCCACAAGGATTTTGATGTCAAAGAGACTTTCT
TCAATTTATCCAAGAGGTATTTTGATACAGAGTGCCTGCCTATGAATTTTCGCAATGCCTCA
CAGGCCAAAAGGCTCATGAATCATTACATTAAACAAAGAGACTCGGGGAAAATTCCCAAAC
GTTTGATGAGATTAATCCTGAAACCAAATTAATTTCTGTGGATTACATCTTGTTCAAAGGGA
AATGGTTGACCCATTTGACCCTGTCTTCACCGAAGTCGACACTTTCCACCTGGACAAGTAC
AAGACCATTAAGGTGCCCATGATGTACGGTGCAGGCAAGTTTGCCTCCACCTTTGACAAGAA
TTTTCGTTGTATGTCTCAAACCTGCCCTACCAAGGAAATGCCACCATGCTGGTGGTCTCA
TGGAGAAAATGGGTGACCACCTCGCCCTTGAAGACTACCTGACCACAGACTTGGTGGAGACA
TGGCTCAGAAAACATGAAAACAGAAACATGGAAGTTTTCTTCCGAAGTTCAAGCTAGATCA
GAAGTATGAGATGCATGAGCTGCTTAGGCAGATGGGAATCAGAAGAATCTTCTCACCCTTTG
CTGACCTTAGTGAACTCTCAGCTACTGGAAGAAATCTCCAAGTATCCAGGGTTTTACGAAGA
ACAGTGATTGAAGTTGATGAAAGGGGCACTGAGGCAGTGGCAGGAATCTTGTGAGAAATTAC
TGCTTATTCATGCCTCCTGTATCAAAGTGGACCGGCCATTTCAATTCATGATCTATGAAG
AAACCTCTGGAATGCTTCTGTTTCTGGGCAGGGTGGTGAATCCGACTCTCCTATTAATTCAGG
ACATGCATAAGCACTTCGTGCTGTAGTAGATGCTGAATCTGAGGTATCAAACACACACAGGA
TACCAGCAATGGATGGCAGGGGAGAGTGTTCTTTTGTCTTAACTAGTTTAGGGTGTCTC
AAATAAATACAGTAGTCCCCACTTATCTGAGGGGGATACATTCAAAGACCCCCAGCAGATGC
CTGAAACGGTGGACAGTGCTGAACCTTATATATATTTTTTCTACACATACATACCTATGAT
AAAGTTTAAATTTATAAATTAGGCACAGTAAGAGATTAACAATAATAACAACATTAAGTAAAA
TGAGTTACTTGAACGCAAGCACTGCAATACCATAACAGTCAAACCTGATTATAGAGAAGGCTA
CTAAGTGACTCATGGGCGAGGAGCATAGACAGTGTGGAGACATTGGGCAAGGGGAGAAATTC
CATCCTGGGTGGGACAGAGCAGGACGATGCAAGATTCATCCCCTACTCAGAATGGCATGC
TGCTTAAGACTTTTAGATTGTTTTATTTCTGGAATTTTTCATTTAATGTTTTTGGACCATGGT
TGACCATGGTTAACTGAGACTGCAGAAAGCAAAACCATGGATAAGGGAGGACTACTACAAAA
GCATTAAATTGATACATATTTTTTAAAAAAAAAAAAAAAAAAAA

FIGURE 292

MKVVP S L L L S V L L A Q V W L V P G L A P S P Q S P E T P A P Q N Q T S R V V Q A P R E E E E D E Q E A S E E K A G E
E E K A W L M A S R Q Q L A K E T S N F G F S L L R K I S M R H D G N M V F S P F G M S L A M T G L M L G A T G P T E T Q I
K R G L H L Q A L K P T K P G L L P S L F K G L R E T L S R N L E L G L S Q G S F A F I H K D F D V K E T F F N L S K R Y F
D T E C V P M N F R N A S Q A K R L M N H Y I N K E T R G K I P K L F D E I N P E T K L I L V D Y I L F K G K W L T P F D P
V F T E V D T F H L D K Y K T I K V P M M Y G A G K F A S T F D K N F R C H V L K L P Y Q G N A T M L V V L M E K M G D H L
A L E D Y L T T D L V E T W L R N M K T R N M E V F F P K F K L D Q K Y E M H E L L R Q M G I R R I F S P F A D L S E L S A
T G R N L Q V S R V L R R T V I E V D E R G T E A V A G I L S E I T A Y S M P P V I K V D R P F H F M I Y E E T S G M L L F
L G R V V N P T L L

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FIGURE 293

CTGGGATCAGCCACTGCAGCTCCCTGAGCACTCTCTACAGAGACGCGGACCCCAGACATGAG
GAGGCTCCTCCTGGTCACCAGCCTGGTGGTTGTGCTGCTGTGGGAGGCAGGTGCAGTCCCAG
CACCCAAGGTCCCTATCAAGATGCAAGTCAAACACTGGCCCTCAGAGCAGGACCCAGAGAAG
GCCTGGGGCGCCCGTGTGGTGGAGCCTCCGGAGAAGGACGACCAGCTGGTGGTGTCTGTTCCC
TGTCAGAAAGCCGAAACTCTTGACCACCGAGGAGAAGCCACGAGGTCAGGGCAGGGGCCCCA
TCCTTCCAGGCACCAAGGCCTGGATGGAGACCGAGGACACCCTGGGCCGTGTCCTGAGTCCC
GAGCCCGACCATGACAGCCTGTACCACCCTCCGCCTGAGGAGGACCAGGGCGAGGAGAGGCC
CCGGTTGTGGGTGATGCCAAATCACCAGGTGCTCCTGGGACCGGAGGAAGACCAAGACCACA
TCTACCACCCCCAGTAGGGCTCCAGGGGCCATCACTGCCCCCGCCCTGTCCCAAGGCCCAGG
CTGTTGGGACTGGGACCCTCCCTACCCTGCCCCAGCTAGACAAATAAACCCAGCAGGCAAA
AAAAAAAAAAAAAAAAA

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FIGURE 294

MRLLLLVTSLVVLLWEAGAVPAPKVPIKMQVKHWPSEQDPEKAWGARVVEPPEKDDQLVVL
FPVQKPCLLTTEEKPRGQGRGPILPGTKAWMETEDTLGRVLSPEPDHDSLYHPPPEEDQGEE
RRLWVMPNHQVLLGPEEDQDHIYHPQ

FIGURE 295

AGAAAGCTGCACTCTGTTGAGCTCCAGGGCGCAGTGGAGGGAGGGAGTGAAGGAGCTCTCTG
TACCCAAGGAAAGTGCAGCTGAGACTCAGACAAGATTACAATGAACCAACTCAGCTTCCTGC
TGTTTCTCATAGCGACCACCAGAGGATGGAGTACAGATGAGGCTAATACTTACTTCAAGGAA
TGGACCTGTTCTTCGTCTCCATCTCTGCCCAGAAAGCTGCAAGGAAATCAAAGACGAATGTCC
TAGTGCAATTTGATGGCCTGTATTTTCTCCGCACTGAGAATGGTGTATCTACCAGACCTTCT
GTGACATGACCTCTGGGGGTGGCGGCTGGACCCTGGTGGCCAGCGTGCATGAGAATGACATG
CGTGGGAAGTGCACGGTGGGCGATCGCTGGTCCAGTCAGCAGGGCAGCAAAGCAGACTACCC
AGAGGGGGACGGCAACTGGGCCAACTACAACACCTTTGGATCTGCAGAGGCGGCCACGAGCG
ATGACTACAAGAACCCTGGCTACTACGACATCCAGGCCAAGGACCTGGGCATCTGGCACGTG
CCCAATAAGTCCCCCATGCAGCACTGGAGAAACAGCTCCCTGCTGAGGTACCGCACGGACAC
TGGCTTCCTCCAGACACTGGGACATAATCTGTTTGGCATCTACCAGAAATATCCAGTGAAAT
ATGGAGAAGGAAAGTGTGGACTGACAACGGCCCGGTGATCCCTGTGGTCTATGATTTTGGC
GACGCCCAGAAAACAGCATCTTATTACTCACCTATGGCCAGCGGAATTCACTGCGGGATT
TGTTCAAGTTCAGGGTATTTAATAACGAGAGAGCAGCCAACGCCTTGTGTGCTGGAATGAGGG
TCACCGGATGTAACACTGAGCATCACTGCATTGGTGGAGGAGGATACTTTCCAGAGGCCAGT
CCCCAGCAGTGTGGAGATTTTCTGGTTTTGATTGGAGTGGATATGGAACTCATGTTGGTTA
CAGCAGCAGCCGTGAGATAACTGAGGCAGCTGTGCTTCTATTCTATCGTTGAGAGTTTTGTG
GGAGGGAACCCAGACCTCTCCTCCCAACCATGAGATCCCAAGGATGGAGAACAACCTTACCCA
GTAGCTAGAATGTTAATGGCAGAAGAGAAAACAATAAATCATATTGACTCAAGAAAAAAA

FIGURE 296

MNQLSFLLFLIATTRGWSTDEANTYFKEWTCSSSPSLPRSCKEIKDECPSAFDGLYFLRTEN
GVIYQTFCDMTSGGGGWTLVASVHENDMRGKCTVGDRWSSQQGSKADYPEGDGNWANYNTFG
SAEAATSDDYKNPGYYDIQAKDLGIWHVPNKSPMQHWRNSSLLRYRTDTGFLQTLGHNLFGI
YQKYPVKYGEKGCWTDNGPVI PVVYDFGDAQKTASYSPYGQREFTAGFVQFRVFNNERAAN
ALCAGMRVTGCNTEHHCIGGGGYFPEASPPQCGDFSGFDWSGYGTHVGYSSSREITEAAVLLFYR

FIGURE 297

GCGGAGCCGGCGCCGGCTGCGCAGAGGAGCCGCTCTCGCCGCCGCCACCTCGGCTGGGAGCC
CACGAGGCTGCCGCATCCTGCCCTCGGAACAATGGGACTCGGCGCGCGAGGTGCTTGGGCCG
CGCTGCTCCTGGGGACGCTGCAGGTGCTAGCGCTGCTGGGGGCCGCCCATGAAAGCGCAGCC
ATGGCGGCATCTGCAAAACATAGAGAATTCTGGGCTTCCACACAACCTCCAGTGCTAACTCAAC
AGAGACTCTCCAACATGTGCCTTCTGACCATACAAATGAAACTTCCAACAGTACTGTGAAAC
CACCAACTTCAGTTGCCTCAGACTCCAGTAATACAACGGTCACCACCATGAAACCTACAGCG
GCATCTAATACAACAACACCAGGGATGGTCTCAACAAATATGACTTCTACCACCTTAAAGTC
TACACCCAAAACAACAAGTGTTTCACAGAACACATCTCAGATATCAACATCCACAATGACCG
TAACCCACAATAGTTCAGTGACATCTGCTGCTTCATCAGTAACAATCACAACAACCTATGCAT
TCTGAAGCAAAGAAAGGATCAAATTTGATACTGGGAGCTTTGTTGGTGGTATTGTATTAAAC
GCTGGGAGTTTTATCTATTCTTTACATTGGATGCAAAATGTATTACTCAAGAAGAGGCATTC
GGTATCGAACCATAGATGAACATGATGCCATCATTTAAGGAAATCCATGGACCAAGGATGGA
ATACAGATTGATGCTGCCCTATCAATTAAATTTGGTTTATTAATAGTTTAAAAACAATATTCT
CTTTTTGAAAATAGTATAAACAGGCCATGCATATAATGTACAGTGTATTACGTAAATATGTA
AAGATTCTTCAAGGTAACAAGGGTTTGGGTTTTGAAATAAACATCTGGATCTTATAGACCGT
TCATACAATGGTTTTAGCAAGTTCATAGTAAGACAAACAAGTCCTATCTTTTTTTTTTGGCT
GGGGTGGGGGCATTGGTCACATATGACCAGTAATTGAAAGACGTCATCACTGAAAGACAGAA
TGCCATCTGGGCATACAAATAAGAAGTTTGTACAGCACTCAGGATTTTGGGTATCTTTTGT
AGCTCACATAAAGAACTTCAGTGCTTTTCAGAGCTGGATATATCTTAATTACTAATGCCACA
CAGAAATTATACAATCAAACCTAGATCTGAAGCATAATTTAAGAAAAACATCAACATTTTTTG
TGCTTTAACTGTAGTAGTTGGTCTAGAAACAAAATACTCC

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FIGURE 298

MGLGARGAWAALLLGTLQVLALLGAAHESAAMAASANIENSGLPNSSANSTETLQHVP
SDH
TNETSNSTVKPPTSVASDSSNTTVTTMKPTAASNTTTPGMVSTNMTSTTLKSTPKTTSV
SQN
TSQISTSTMTVTHNSSVTSAASSVTITTTMHSEAKKGSKFDTGSFVGGIVLTLGVLSI
LYIG
CKMYYSRRGIRYRTIDEHDAII

FIGURE 299

CAGCCGGGTCCCAAGCCTGTGCCTGAGCCTGAGCCTGAGCCTGAGCCCGAGCCGGGAGCCGG
TCGCGGGGGCTCCGGGCTGTGGGACCGCTGGGCCCCCAGCGATGGCGACCCTGTGGGGAGGC
CTTCTTCGGCTTGGCTCCTTGCTCAGCCTGTGCTGCCTGGCGCTTCCGTGCTGCTGCTGGC
GCAGCTGTCAGACGCCGCCAAGAATTTGAGGATGTCAGATGTAAATGTATCTGCCCTCCCT
ATAAAGAAAATTCTGGGCATATTTATAATAAGAACATATCTCAGAAAGATTGTGATTGCCTT
CATGTTGTGGAGCCCATGCCTGTGCGGGGGCCTGATGTAGAAGCATACTGTCTACGCTGTGA
ATGCAAATATGAAGAAAGAAGCTCTGTCACAATCAAGGTTACCATTATAATTTATCTCTCCA
TTTTGGGCCTTCTACTTCTGTACATGGTATATCTTACTCTGGTTGAGCCCATACTGAAGAGG
CGCCTCTTTGGACATGCACAGTTGATACAGAGTGATGATGATATTGGGGATCACCAGCCTTT
TGCAAATGCACACGATGTGCTAGCCCGCTCCCGCAGTCGAGCCAACGTGCTGAACAAGGTAG
AATATGCACAGCAGCGCTGGAAGCTTCAAGTCCAAGAGCAGCGAAAGTCTGTCTTTGACCGG
CATGTTGTCTCAGCTAATTGGGAATTGAATTCAAGGTGACTAGAAAGAAACAGGCAGACAA
CTGGAAGAAGTACTGAGTGGGTTTTGCTGGGTTTCATTTTAATACCTTGTTGATTTTACCAACT
GTTGCTGGAAGATTCAAAAGTGAAGCAAAAAGTCTTGCTTGATTTTTTTTTTCTTGTTAACGTA
ATAATAGAGACATTTTTTAAAAGCACACAGCTCAAAGTCAGCCAATAAGTCTTTTTCTATTTG
TGACTTTTACTAATAAAAATAAATCTGCCTGTAAATTATCTTGAAGTCCTTTACCTGGAACA
AGCACTCTCTTTTTTACCACATAGTTTTAACTTGACTTTCAAGATAATTTTTCAGGGTTTTTG
TTGTTGTTGTTTTTTGTTTGTGTTTGGTGGGAGAGGGGAGGGATGCCTGGGAAGTGGTT
AACAAGTTTTTTCAAGTCACTTTACTAAACAACTTTTGTAATAGACCTTACCTTCTATTT
TCGAGTTTCATTTATATTTTGCAGTGTAGCCAGCCTCATCAAAGAGCTGACTTACTCATTTG
ACTTTTGCACTGACTGTATTATCTGGGTATCTGCTGTGTCTGCACTTCATGGTAAACGGGAT
CTAAAATGCCTGGTGGCTTTTCAAAAAAGCAGATTTTCTTCATGTACTGTGATGTCTGATG
CAATGCATCCTAGAACAACTGGCCATTTGCTAGTTTACTCTAAAGACTAAACATAGTCTTG
GTGTGTGTGGTCTTACTCATCTTCTAGTACCTTTAAGGACAAATCCTAAGGACTTGGACACT
TGCAATAAAGAAATTTTATTTTAAACCAAGCCTCCCTGGATTGATAATATATACACATTTG
TCAGCATTTCCGGTCGTGGTGAGAGGCAGCTGTTTGAGCTCCAATATGTGCAGCTTTGAACT
AGGGCTGGGGTTGTGGGTGCCTCTTCTGAAAGGTCTAACCATTATTGGATAACTGGCTTTTT
TCTTCTATGTCCTCTTTGGAATGTAACAATAAAAATAATTTTGAACATCAA

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FIGURE 300

MATLWGGLRLGSLLSLSCLALSVLLLAQLSDAAKNFEDVRCKCICPPYKENS
GHIYNKNIS
QKDCDCLHVVEPMPVRGPDVEAYCLRCECKYEERSSVTIKVTII IYLSILGLLLLYMVYLT
L
VEPILKRRLFGHAQLIQSDDDIGDHQPFANAHDVLA
RSRANVLNKVEYAQQRWKLQVQEQ
RKSVFDRHVVL

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FIGURE 301

GCACCTGCGACCAACCGTGAGCAGTCAATGGCGTACTCCACAGTGCAGAGAGTCGCTCTGGCTT
CTGGGCTTGTCCTGGCTCTGTGCTGCTGCTGCCCAAGGCCTTCCTGTCCCGCGGGAAGCGG
CAGGAGCCGCCGCCGACACCTGAAGGAAAATTGGGCCGATTTCCACCTATGATGCATCATCA
CCAGGCACCCTCAGATGGCCAGACTCCTGGGGCTCGTTTTCCAGAGGTCTCACCTTGCCGAGG
CATTTGCAAAGGCCAAAGGATCAGGTGGAGGTGCTGGAGGAGGAGGTAGTGGAAGAGGTCTG
ATGGGGCAGATTATTCCAATCTACGGTTTTGGGATTTTTTTATATATACTGTACATTCTATT
TAAGGTAAGTAGAATCATCCTAATCATATTACATCAATGAAAAATCTAATATGGCGATAAAAA
TCATTGTCTACATTAAAACTTCTTATAGTTCATAAAATTATTTCAAATCCATCATCTCTTTA
AATCCTGCCTCCTCTTCATGAGGTACTTAGGATAGCCATTATTTCAGTTTCACATAAGAATG
TTTACTCAATGTTTAAAGTGTTTTGCCCCAAAATTCACAACTAACAAGGCAGAACTAGGACTT
GAACATGGATCTTTTGGTTCTTAATCCAGTGAGTGATACAATTCAATGCACTCCCCTGCCA

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FIGURE 302

MAYSTVQRVALASGLVLALSLLLPKAFLSRGKRQEPPTPEGKLGRFPPMMHHHQAPSDGQT
PGARFQRSHLAEAFKAKGSGGGAGGGGSGRGLMGQIIPYGFIFYILFKVSRIILI
ILHQ

FIGURE 303

CGGCTCGAGTGCAGCTGTGGGGAGATTTCACTGCATTGCCTCCCCTGGGTGCTCTTCATCTT
GGATTTGAAAGTTGAGAGCAGCATGTTTTGCCCCTGAAACTCATCCTGCTGCCAGTGTTAC
TGGATTATTCCTTGGGCCTGAATGACTTGAATGTTTTCCCCGCCTGAGCTAACAGTCCATGTG
GGTGATTCAAGCTCTGATGGGATGTGTTTTCCAGAGCACAGAAGACAAATGTATATTCAAGAT
AGACTGGACTCTGTACCAGGAGAGCACGCCAAGGACGAATATGTGCTATACTATTACTCCA
ATCTCAGTGTGCCTATTGGGCGCTTCCAGAACCGCGTACACTTGATGGGGGACATCTTATGC
AATGATGGCTCTCTCCTGCTCCAAGATGTGCAAGAGGCTGACCAGGGAACCTATATCTGTGA
AATCCGCCTCAAAGGGGAGAGCCAGGTGTTCAAGAAGGCGGTGGTACTGCATGTGCTTCCAG
AGGAGCCCCAAGAGCTCATGGTCCATGTGGGTGGATTGATTGAGATGGGATGTGTTTTCCAG
AGCACAGAAGTGAAACACGTGACCAAGGTAGAATGGATATTTTCAGGACGGCGCGCAAAGGA
GGAGATTGTATTTTCGTTACTACCACAACTCAGGATGTCTGTGGAGTACTCCCAGAGCTGGG
GCCACTTCCAGAATCGTGTGAACCTGGTGGGGGACATTTTCCGCAATGACGGTTCCATCATG
CTTCAAGGAGTGAGGGAGTCAGATGGAGGAACTACACCTGCAGTATCCACCTAGGGAACCT
GGTGTTCAGAAAACCATTTGTGCTGCATGTGAGCCCGGAAGAGCCTCGAACACTGGTGACCC
CGGCAGCCCTGAGGCCTCTGGTCTTGGGTGGTAATCAGTTGGTGATCATTGTGGGAATTGTC
TGTGCCACAATCCTGCTGCTCCCTGTTCTGATATTGATCGTGAAGAAGACCTGTGGAAATAA
GAGTTCAGTGAATTCTACAGTCTTGGTGAAGAACACGAAGAAGACTAATCCAGAGATAAAAG
AAAAACCCTGCCATTTTGAAAGATGTGAAGGGGAGAAACACATTTACTCCCCAATAATTGTA
CGGGAGGTGATCGAGGAAGAAGAACCAAGTGAAAAATCAGAGGCCACCTACATGACCATGCA
CCCAGTTTGGCCTTCTCTGAGGTGAGATCGGAACAACTCACTTGAAAAAAGTCAGGTGGGG
GAATGCCAAAAACACAGCAAGCCTTTTGAGAAGAATGGAGAGTCCCTTCATCTCAGCAGCGG
TGGAGACTCTCTCCTGTGTGTGCTTGGGCCACTCTACCAGTGATTTGAGACTCCCGCTCTC
CCAGCTGTCTCCTGTCTCATTGTTTGGTCAATACACTGAAGATGGAGAATTTGGAGCCTGG
CAGAGAGACTGGACAGCTCTGGAGGAACAGGCCTGCTGAGGGGAGGGGAGCATGGACTTGGC
CTCTGGAGTGGGACACTGGCCCTGGGAACAGGCTGAGCTGAGTGGCCTCAAACCCCCGTT
GGATCAGACCCTCCTGTGGGCAGGGTTCTTAGTGGATGAGTTACTGGGAAGAATCAGAGATA
AAAACCAACCCAAATCAA

FIGURE 304

MFCPLKLILLPVLLDYSGLNDLNVSPPELTVHVGDSALMGCVFQSTEDKCIFKIDWTLSPG
EHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDILCNDGSLLLQDVQEADQGTYICEIRLKGES
QVFKKAVVLHVLPEEPKELMVHVGGLIQMGCVFQSTEVKHVTKVEWIFSGRRAKEEIVFRYY
HKLMSVEYSQSWG HFQNRVNLVGDI FRNDGSIMLQGVRES DGGNYTCSIHLGNLVFKKTIV
LHVSPEEPRTLVT PAALRPLVLGGNQLV IIVGIVCATILLLPVLILIVKKT CGNKSSVNSTV
LVKNTKKTNP EIKEKPCHFERCEGEKHIYSPI IIVREVI EEEEPSEKSEATYMTMHPVWPSLR
SDRNNSLEKKSGGGMPKTQQAF

FIGURE 305

CTATGAAGAAGCTTCCTGGAAAACAATAAGCAAAGGAAAACAAATGTGTCCCATCTCACATG
GTTCTACCCTACTAAAGACAGGAAGATCATAACTGACAGATACTGAAATTGTAAGAGTTGG
AAACTACATTTTGC AAAGTCATTGAACTCTGAGCTCAGTTGCAGTACTCGGGAAGCCATGCA
GGATGAAGATGGATACATCACCTTAAATATTAAAACCTCGGAAACCAGCTCTCGTCTCCGTTG
GCCCTGCATCCTCCTCCTGGTGGCGTGTGATGGCTTTGATTCTGCTGATCCTGTGCGTGGGG
ATGGTTGTCTGGGCTGGTGGCTCTGGGGATTTGGTCTGTCTATGCAGCGCAATTACCTACAAGA
TGAGAATGAAAATCGCACAGGAACCTCTGCAACAATTAGCAAAGCGCTTCTGTCAATATGTGG
TAAAACAATCAGAACTAAAGGGCACTTTCAAAGGTCATAAATGCAGCCCCCTGTGACACAAAC
TGGAGATATTATGGAGATAGCTGCTATGGGTTCTTCAGGCACAACCTAACATGGGAAGAGAG
TAAGCAGTACTGCACTGACATGAATGCTACTCTCCTGAAGATTGACAACCGGAACATTGTGG
AGTACATCAAAGCCAGGACTCATTTAATTCGTTGGGTCGGATTATCTCGCCAGAAGTCTGAAT
GAGGTCTGGAAGTGGGAGGATGGCTCGGTTATCTCAGAAAATATGTTTGAGTTTTTGAAGA
TGGAAAAGGAAATATGAATTGTGCTTATTTTCATAATGGGAAAATGCACCCTACCTTCTGTG
AGAACAAACATTATTTAATGTGTGAGAGGAAGGCTGGCATGACCAAGGTGGACCAACTACCT
TAATGCAAAGAGGTGGACAGGATAACACAGATAAGGGCTTTATTGTACAATAAAAGATATGT
ATGAATGCATCAGTAGCTGAAAAAAAAAAAAA

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FIGURE 306

MQDEDGYITLNIKTRKPALVSVGPASSSWVRMALILLILCVGMVVGLVALGIWSVMQRNYL
QDENENRTGTLQQLAKRFCQYVVKQSELKGTFFKGHKCSPCDTNWRYYGDSYGFRRHNLWE
ESKQYCTDMNATLLKIDNRNIVEYIKARTHLIRWVGLSRQKSNEVWKWEDGSVISENMFEDL
EDGKGNMNCAYFHNGKMHPTFCENKHYLMCERKAGMTKVDQLP

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|-----------------|----------------------------------|----|-----------------|----------------------------------|----|-----------------|----------------------------------|----|
| (30) 60/088,742 | 10 Jun/juin 1998 (10.06.1998) | US | (30) 60/090,254 | 22 Jun/juin 1998 (22.06.1998) | US | (30) 60/091,478 | 2 Jul/jul 1998 (02.07.1998) | US |
| (30) 60/088,810 | 10 Jun/juin 1998 (10.06.1998) | US | (30) 60/090,355 | 23 Jun/juin 1998 (23.06.1998) | US | (30) 60/091,626 | 2 Jul/jul 1998 (02.07.1998) | US |
| (30) 60/088,811 | 10 Jun/juin 1998 (10.06.1998) | US | (30) 60/090,349 | 23 Jun/juin 1998 (23.06.1998) | US | (30) 60/091,628 | 2 Jul/jul 1998 (02.07.1998) | US |
| (30) 60/088,824 | 10 Jun/juin 1998 (10.06.1998) | US | (30) 60/090,429 | 24 Jun/juin 1998 (24.06.1998) | US | (30) 60/091,633 | 2 Jul/jul 1998 (02.07.1998) | US |
| (30) 60/088,825 | 10 Jun/juin 1998 (10.06.1998) | US | (30) 60/090,431 | 24 Jun/juin 1998 (24.06.1998) | US | (30) 60/091,646 | 2 Jul/jul 1998 (02.07.1998) | US |
| (30) 60/088,826 | 10 Jun/juin 1998 (10.06.1998) | US | (30) 60/090,435 | 24 Jun/juin 1998 (24.06.1998) | US | (30) 60/091,673 | 2 Jul/jul 1998 (02.07.1998) | US |
| (30) 60/088,858 | 11 Jun/juin 1998 (11.06.1998) | US | (30) 60/090,444 | 24 Jun/juin 1998 (24.06.1998) | US | (30) 60/091,978 | 7 Jul/jul 1998 (07.07.1998) | US |
| (30) 60/088,861 | 11 Jun/juin 1998 (11.06.1998) | US | (30) 60/090,445 | 24 Jun/juin 1998 (24.06.1998) | US | (30) 60/091,982 | 7 Jul/jul 1998 (07.07.1998) | US |
| (30) 60/088,863 | 11 Jun/juin 1998 (11.06.1998) | US | (30) 60/090,461 | 24 Jun/juin 1998 (24.06.1998) | US | (30) 60/092,182 | 9 Jul/jul 1998 (09.07.1998) | US |
| (30) 60/088,876 | 11 Jun/juin 1998 (11.06.1998) | US | (30) 60/090,472 | 24 Jun/juin 1998 (24.06.1998) | US | (30) 60/092,472 | 10 Jul/jul 1998 (10.07.1998) | US |
| (30) 60/089,090 | 12 Jun/juin 1998 (12.06.1998) | US | (30) 60/090,535 | 24 Jun/juin 1998 (24.06.1998) | US | (30) 60/093,339 | 20 Jul/jul 1998 (20.07.1998) | US |
| (30) 60/089,105 | 12 Jun/juin 1998 (12.06.1998) | US | (30) 60/090,538 | 24 Jun/juin 1998 (24.06.1998) | US | (30) 60/094,651 | 30 Jul/jul 1998 (30.07.1998) | US |
| (30) 60/089,440 | 16 Jun/juin 1998 (16.06.1998) | US | (30) 60/090,540 | 24 Jun/juin 1998 (24.06.1998) | US | (30) 60/095,282 | 4 Aug/aout 1998 (04.08.1998) | US |
| (30) 60/089,512 | 16 Jun/juin 1998 (16.06.1998) | US | (30) 60/090,557 | 24 Jun/juin 1998 (24.06.1998) | US | (30) 60/095,285 | 4 Aug/aout 1998 (04.08.1998) | US |
| (30) 60/089,514 | 16 Jun/juin 1998 (16.06.1998) | US | (30) 60/090,676 | 25 Jun/juin 1998 (25.06.1998) | US | (30) 60/095,301 | 4 Aug/aout 1998 (04.08.1998) | US |
| (30) 60/089,532 | 17 Jun/juin 1998 (17.06.1998) | US | (30) 60/090,678 | 25 Jun/juin 1998 (25.06.1998) | US | (30) 60/095,302 | 4 Aug/aout 1998 (04.08.1998) | US |
| (30) 60/089,538 | 17 Jun/juin 1998 (17.06.1998) | US | (30) 60/090,688 | 25 Jun/juin 1998 (25.06.1998) | US | (30) 60/095,318 | 4 Aug/aout 1998 (04.08.1998) | US |
| (30) 60/089,598 | 17 Jun/juin 1998 (17.06.1998) | US | (30) 60/090,690 | 25 Jun/juin 1998 (25.06.1998) | US | (30) 60/095,321 | 4 Aug/aout 1998 (04.08.1998) | US |
| (30) 60/089,599 | 17 Jun/juin 1998 (17.06.1998) | US | (30) 60/090,691 | 25 Jun/juin 1998 (25.06.1998) | US | (30) 60/095,325 | 4 Aug/aout 1998 (04.08.1998) | US |
| (30) 60/089,600 | 17 Jun/juin 1998 (17.06.1998) | US | (30) 60/090,694 | 25 Jun/juin 1998 (25.06.1998) | US | (30) 60/095,916 | 10 Aug/aout 1998 (10.08.1998) | US |
| (30) 60/089,653 | 17 Jun/juin 1998 (17.06.1998) | US | (30) 60/090,695 | 25 Jun/juin 1998 (25.06.1998) | US | (30) 60/095,929 | 10 Aug/aout 1998 (10.08.1998) | US |
| (30) 60/089,801 | 18 Jun/juin 1998 (18.06.1998) | US | (30) 60/090,696 | 25 Jun/juin 1998 (25.06.1998) | US | (30) 60/096,012 | 10 Aug/aout 1998 (10.08.1998) | US |
| (30) 60/089,907 | 18 Jun/juin 1998 (18.06.1998) | US | (30) 60/090,862 | 26 Jun/juin 1998 (26.06.1998) | US | (30) 60/096,143 | 11 Aug/aout 1998 (11.08.1998) | US |
| (30) 60/089,908 | 18 Jun/juin 1998 (18.06.1998) | US | (30) 60/090,863 | 26 Jun/juin 1998 (26.06.1998) | US | (30) 60/096,146 | 11 Aug/aout 1998 (11.08.1998) | US |
| (30) 60/089,947 | 19 Jun/juin 1998 (19.06.1998) | US | (30) 60/091,358 | 1 Jul/jul 1998 (01.07.1998) | US | (30) 60/096,329 | 12 Aug/aout 1998 (12.08.1998) | US |
| (30) 60/089,948 | 19 Jun/juin 1998 (19.06.1998) | US | (30) 60/091,360 | 1 Jul/jul 1998 (01.07.1998) | US | (30) 60/096,757 | 17 Aug/aout 1998 (17.08.1998) | US |
| (30) 60/089,952 | 19 Jun/juin 1998 (19.06.1998) | US | (30) 60/091,544 | 1 Jul/jul 1998 (01.07.1998) | US | (30) 60/096,766 | 17 Aug/aout 1998 (17.08.1998) | US |
| (30) 60/090,246 | 22 Jun/juin 1998 (22.06.1998) | US | (30) 60/091,486 | 2 Jul/jul 1998 (02.07.1998) | US | (30) 60/096,768 | 17 Aug/aout 1998 (17.08.1998) | US |
| (30) 60/090,252 | 22 Jun/juin 1998 (22.06.1998) | US | (30) 60/091,519 | 2 Jul/jul 1998 (02.07.1998) | US | (30) 60/096,773 | 17 Aug/aout 1998 (17.08.1998) | US |
| | | | | | | (30) 60/096,791 | 17 Aug/aout 1998 (17.08.1998) | US |

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|-----------------|------------------------------------|
| (30) 60/096,867 | 17 Aug/oct 1998 US (17.08.1998) |
| (30) 60/096,891 | 17 Aug/oct 1998 US (17.08.1998) |
| (30) 60/096,894 | 17 Aug/oct 1998 US (17.08.1998) |
| (30) 60/096,895 | 17 Aug/oct 1998 US (17.08.1998) |
| (30) 60/096,897 | 17 Aug/oct 1998 US (17.08.1998) |
| (30) 60/096,949 | 18 Aug/oct 1998 US (18.08.1998) |
| (30) 60/096,950 | 18 Aug/oct 1998 US (18.08.1998) |
| (30) 60/096,959 | 18 Aug/oct 1998 US (18.08.1998) |
| (30) 60/096,960 | 18 Aug/oct 1998 US (18.08.1998) |
| (30) 60/097,022 | 18 Aug/oct 1998 US (18.08.1998) |
| (30) 60/097,141 | 19 Aug/oct 1998 US (19.08.1998) |
| (30) 60/097,218 | 20 Aug/oct 1998 US (20.08.1998) |
| (30) 60/097,661 | 24 Aug/oct 1998 US (24.08.1998) |
| (30) 60/097,951 | 26 Aug/oct 1998 US (26.08.1998) |
| (30) 60/097,952 | 26 Aug/oct 1998 US (26.08.1998) |
| (30) 60/097,954 | 26 Aug/oct 1998 US (26.08.1998) |
| (30) 60/097,955 | 26 Aug/oct 1998 US (26.08.1998) |
| (30) 60/097,971 | 26 Aug/oct 1998 US (26.08.1998) |
| (30) 60/097,974 | 26 Aug/oct 1998 US (26.08.1998) |
| (30) 60/097,978 | 26 Aug/oct 1998 US (26.08.1998) |
| (30) 60/097,979 | 26 Aug/oct 1998 US (26.08.1998) |
| (30) 60/097,986 | 26 Aug/oct 1998 US (26.08.1998) |
| (30) 60/098,014 | 26 Aug/oct 1998 US (26.08.1998) |
| (30) 60/098,525 | 31 Aug/oct 1998 US (31.08.1998) |
| (30) 60/100,634 | 16 Sept 1998 US (16.09.1998) |
| (30) 60/115,565 | 12 Jan 1999 US (12.01.1999) |

